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IMMUNOLOGIC RELATIONSHIPS BETWEEN COW'S MILK AND GOAT'S MILK

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SOME infants who are hypersensitive to cow's milk can tolerate goat's milk; others cannot. The immunologic relationships between the two most important proteins of these milks is therefore not merely of academic interest, but of considerable practical interest.

It has been definitely established by Anderson, Schloss and Stuart and by several other investigators that cow and goat casein are immunologically almost identical.[1, 2, 3] For lactalbumin the situation is not so clear, although it is stated many times in the literature that cow and goat milk lactalbumin are immunologically distinct. These statements are, however, not based upon original work, and I can find no original investigation on the subject, except that by von Versell[4] in 1915. This author, who by means of the complement fixation test in immunized animals did a monumental piece of work on the immunologic relationships of isolated proteins from the milks of several species of animals, wrote as follows: "The antiserum from uncooked and cooked whole cow's milk, casein, and whey reacted strongest with its homologous antigen, somewhat less strongly with the corresponding antigen of goat milk, and still weaker with that of human milk. The species specificity showed itself especially in the whey antiserum, which reacted with goat's milk whey more weakly than with cow's milk whey, and with human whey not at all."

He states clearly here that he found human and cow lactalbumin to be entirely species specific. He did not find that the whey proteins of two such closely related animals as the cow and the goat were sharply and definitely species specific. He found only that they were not identical and showed a somewhat greater specificity than the corresponding caseins. Until we read von Versell's paper in the original, we had

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believed that goat and cow lactalbumin were almost entirely if not entirely species specific. After reading his paper, it became apparent that his findings had been somewhat misinterpreted, and it seemed desirable to go further into the matter, as the question is of some importance in the clinical management of milk sensitive infants.

We tested 44 eczematous infants who gave a positive intracutaneous reaction to a specially purified solution of cow lactalbumin, with a specially purified solution of goat lactalbumin of the same strength (0.16 mg. N).* Ten were entirely negative to goat lactalbumin, 9 gave doubtful reactions, much smaller than those to cow lactalbumin, and 25 gave identical positive reactions to both. That these crossed reactions were due to contamination of the testing solutions with casein seems very unlikely, as nearly half (10) of the group who gave positive reactions to goat lactalbumin gave negative reactions to both cow and goat casein, and, when there was a positive test to casein, it was usually smaller than the reaction to goat lactalbumin.

It seems that the species specificity of the two lactalbumins is not as great as has generally been thought. As a matter of fact, proteins from closely related species often do not show great specificity, particularly if the protein in question has the same specialized function to perform in each species. Hen's egg ovalbumin will sensitize to duck egg ovalbumin and to the egg albumin of many other birds; there are crossed reactions between the pollens of various species of grasses; chemically similar proteins from seeds of different genera will sensitize against each other, as will spermatozoa from different varieties of mammals. There are many antigens, the specificity of which is determined by chemical constitution and function, rather than by species relationships, as Wells and Lewis have particularly emphasized. The theory has been advanced, and in recent years there has developed so much evidence to support it that it may be regarded as established fact rather than theory, that many antigens contain two sensitizing determinants, one species specific, and another common to the antigen in question and to other closely related antigens as well, and that an individual may become sensitized to the species-specific factor alone or to both.[5, 6, 7] This is well illustrated by the infants under discussion. Some are sensitized to the species-specific factor of cow lactalbumin alone and some also to the factor common to both cow and goat lactalbumin; in either of these two groups there may be sensitization to casein as well. In still a third, but very much smaller group there may be sensitization to casein alone.

It is therefore readily seen that goat's milk as a therapeutic agent is indicated only in the first group. This is borne out by clinical expe-

*These preparations were kindly made for us at the Lederle Laboratories under the direction of Dr. Arthur Coca. The Method of Schloss was used (J. A. M. A., March 21, 1936).

rience: occasionally results with goat's milk as a diet for eczematous infants hypersensitive to cow's milk are brilliant; more often such infants are no better off with goat's milk than they are with cow's milk.

In apparent contradiction to these findings is the fact that most infants with the very severe type of cow's milk hypersensitivity, as a rule without eczema, who go into alarming collapse and may even die[8] when they take only a small amount of cow's milk, can take goat's milk with impunity. Such patients are not common; any data concerning them must at present be mostly clinical, and drawn from the experiences of several men over a period of a good many years. We have been able to obtain reliable data on 25 such patients, 5 of whom we saw personally. Of the 25 patients, 15 were fed on goat's milk without symptoms; in the others it was not tried. It is certain that in those infants who can take goat's milk there is no casein sensitivity, and that there is sensitivity to the species-specific determinant of cow lactalbumin alone.

The immunologic situation in many of these infants seems to be somewhat different than in those with eczema. They are not likely to have other sensitivities, and they more often give negative than positive skin tests to milk, in spite of exquisite clinical hypersensitivity. In the serum of the only patient of this type we have been able to examine, atopic antibodies, or reagins, so characteristic of eczema, which could transfer specific sensitivity to the normal human skin, were absent, although the ingestion of only a few drops of cow's milk caused immediate vomiting and collapse. Milk sensitivity in the eczematous infant is very common, but it is rarely of such degree or quality that the infant is sent into shock by taking milk. If it is of such degree, strongly positive skin tests to both cow and goat milk are likely to be present. Tisdall and Erb's two cases and Ashby's case (Table I) were all so hypersensitive to cow's milk that they could take none of it.

All three had eczema and strongly positive skin tests to both cow and goat milk. Our four patients without eczema were equally hypersensitive. Skin tests were done on three, and were negative. Two of these were fed goat's milk without difficulty. In the other it was not tried. Our one patient with eczema had strongly positive skin tests to both cow and goat milk, could take no cow's milk without vomiting, hives and shock, and was fed a milk-free food. Coca and Grove[9] have reported somewhat analogous findings: an individual who was so hypersensitive to peas that her lips immediately became swollen if she took the smallest amount of pea in her mouth and who would undoubtedly have been shocked if she actually ate any considerable amount of it. She had, however, negative skin tests, and no reagins to pea in her serum. Another individual, in whom sensitization to peas was a contributing factor in producing *asthma*, had a positive skin test to pea, and atopic reagins in his serum.

Eczematous infants are very commonly sensitive to egg white. If they are so hypersensitive, and they often are, that ingestion or injection of egg will produce shock, positive skin tests to egg, and atopic reagins are almost invariably present.

TABLE I

PHYSICIAN	SKIN TESTS	SUCCESSFUL FEEDING
Kerley[1]	Neg.	Goat milk
"	Neg.	Goat milk
"	Neg.	Goat milk
"	Neg.	Goat milk
"	Neg.	Goat milk
"	Neg.	
"	Neg.	
"	Pos.	
"	Pos.	
Hill	Neg.	Human milk
"	Neg.	Goat milk
"	Neg.	Human milk
		Goat milk
"	Pos.	Sobee
Talbot[2]	Slightly pos.	Goat milk
"		Goat milk
Park[3]	Neg.	Goat milk
Carmichael[4]	Neg.	Goat milk
Ashby[5]	Pos. cow milk. Pos. goat milk	
Tisdall and Erb[6]	Pos. cow milk. Pos. goat milk	
" "	Pos. cow milk. Pos. goat milk	
J. L. Morse[1]		Goat milk
R. M. Smith[1]		Goat milk
"		Goat milk
Cumming[7]	Slightly pos.	Goat milk

All of these infants reacted with such violent symptoms to the ingestion of a very small quantity of cow's milk, so that as a diet for them it was out of the question. Those for whom goat milk was not tried were either kept on the breast and gradually desensitized to cow's milk, or were fed on a milk-free food.

[1]Personal communication.
[2]Boston Med. & S. J. 175: 409, 1916.
[3]Am. J. Dis. Child. 19: 496, 1920.
[4]Arch. Dermat. & Syph. 2: 544, 1920.
[5]Arch. Dis. Child. 4: 264, 1929.
[6]Canad. M. A. J. 13: 497, 1929.
[7]Arch. Dis. Child. 3: 296, 1928.

In short, there are scattered bits of evidence which suggest that those infants who suffer shock from the ingestion of cow's milk, but have no positive skin tests and no eczema, may not belong in quite the same immunologic group as those with eczema. This does not seem surprising, for conditions of antigenic exposure are very different in the two groups. The "shock" cases are breast-fed infants who have had no cow's milk except possibly a few feedings during the neonatal period, and when offered it, usually several months after the first exposure, react with such violent symptoms that cow's milk as a diet is quite impossible. It is also possible that the sensitization may be either truly hereditary or

congenital. The bottle-fed milk-sensitive eczematous infant, on the other hand, has been taking large amounts of cow's milk every day for months, and thrives on it.

In animals the time interval between antigenic exposures determines to a considerable degree the type of immunologic reaction that will take place. Manwaring,[10] for example, found that dogs injected with a few doses of horse serum, after a proper interval could be easily shocked, but, if the number of doses was considerably increased and given at frequent and regular intervals, they could not be shocked. Schloss[11] and Wells[12] have found essentially the same thing with guinea pigs when the antigens were given by mouth.

There is much discussion and much difference of opinion among allergists and immunologists as to whether the atopic reagin or antibody so often associated with the so-called atopic diseases, asthma, hay fever, and eczema, is identical with the anaphylactic antibody of animal anaphylaxis. Some believe that they are identical; some that they are different antibodies. A detailed discussion of this complicated question would be out of place here, but from the somewhat meager evidence available it seems that the situation of the infants in question with no eczema and negative skin tests more closely resembles that of the anaphylactic animal than it does that of the asthma, eczema, hay fever group.

This may possibly explain why most of them have a sharply defined sensitization to the species-specific antigenic factor of cow lactalbumin alone, for it has been found[13, 14] that the anaphylactic antibody is more highly specific, and is less likely to react with related antigens than is the atopic reagin or skin sensitizing antibody characteristic of asthma, eczema, and hay fever. Furthermore, Wolfe[15] has shown that the interval between antigenic exposure and the number of exposures has a great deal to do with determining the specificity of the resulting antibodies.

At any rate, leaving out all the highly perplexing and controversial definitions of immunologic dialectics, and returning to plain English, these babies are much more likely to be able to drink goat's milk without harm than is the eczematous infant with the ordinary type of cow's milk hypersensitivity, who can do so only occasionally.

CONCLUSIONS

1. There is more species specificity between cow and goat lactalbumin than there is between cow and goat casein, but they are by no means entirely species specific.

2. The skin sensitizing antibody characteristic of eczema in the infant will often give crossed reactions with cow and goat lactalbumin. The undetermined antibody of severe milk idiosynerasy without eczema is not likely to do this.

3. Goat's milk has a definite and valuable place in the treatment of some, but by no means all, infants with hypersensitivity to cow's milk.

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ACUTE COCCIDIOIDOMYCOSIS WITH ERYTHEMA NODOSUM IN CHILDREN

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COCCIDIOIDAL granuloma, a chronic progressive disease affecting skin, bones, lungs, and meninges, has been known to the medical world since 1892.[1-6] It has a mortality of about 50 per cent. The causative agent, the fungus *Coccidioides immitis,* has been recognized since 1896.[4] That the same fungus is also the cause of an entirely different clinical syndrome with an acute course ending in complete recovery in practically all cases was not clearly proved and brought to the attention of the medical profession until 1937 when Dickson[7] published the first of his careful studies[7-10] on the subject, one of them in collaboration with Gifford.[8] To this syndrome Dickson has applied the term "primary or acute coccidioidomycosis" to emphasize its differences from the chronic disease.

The clinical picture of the acute disease has long been known to physicians of the San Joaquin Valley under such names as "valley fever," "San Joaquin fever" and "desert fever," and one of its common manifestations, erythema nodosum, is familiar to the laity of that region as "the bumps." The acute disease, unlike coccidioidal granuloma, is common among children, occurring even during infancy, but has not hitherto been described in the pediatric literature. The present report is based on 24 cases, personally studied, in children under 15 years of age.

CAUSATIVE AGENT

The coccidioides fungus occurs in two forms or cycles: one, the vegetative form which is found in culture and presumably in nature; the other, the parasitic form, which is found in infected tissues.[11-16] On culture media, hyphae are formed which bear chlamydospores; with aging these fragments are easily transported through the air. That the spores are infectious has been definitely proved by the occurrence of infections in laboratory workers in at least two instances. There is good reason to suppose that the disease is as a rule spread by dust contaminated with chlamydospores and inhaled.[17, 18, 6, 8]

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In infected tissues and sputum, the organism appears as a double contoured spherule about 30μ in diameter, which is easily recognized in fresh, wet preparations and so provides a means of tentative diagnosis. Since person-to-person transmission of infection is unknown, it is supposed that the spherule form is not transmissible, but the point deserves further study.

EPIDEMIOLOGY

Coccidioidal disease is largely confined to the San Joaquin Valley, the southern component of the great central valley of California, although sporadic cases are also known to occur in Arizona.[19, 20, 21] However, it must be admitted that under modern conditions of travel and, particularly, of labor migration patients with coccidioidomycosis may be encountered anywhere in the country. Clinicians and pathologists should be aware of this possibility and, if the diagnosis is established, should inquire carefully as to past residence. Another endemic center exists in Argentina,[1, 2] and Jaccono isolated coccidioides from two Neapolitan silo workers who had never been outside Italy.[22 a, b]

The known foci in California and Arizona have in common a semiarid climate where irrigation is necessary. As Dickson[16] has pointed out, the fungus is found where the winters are relatively warm, rainfall sparse, and summers hot and dry with much dust. Although patients develop coccidioidomycosis throughout the year the incidence is least during the rainy season and greatest in the late autumn and early winter before the rains.[23] Of our 24 cases, 3 began in the spring, 7 in the summer, 12 in the autumn and 2 in the winter.

No age is spared. In Dickson's questionnaire,[8] 3 per cent of the patients were under school age and 18 per cent were of school age. Gifford, Buss, and Douds[6] found 26 per cent of their 104 patients with "San Joaquin Fever" to be under 20 years of age. They also pointed out that while the age distribution of these patients corresponded to that of victims of coccidioidal granuloma females outnumbered males by 2:1 (the same figure as that obtained by Dickson) while with coccidioidal granuloma males outnumbered females by 4:1. In our series, however, of 22 patients with erythema nodosum, 12 were girls and 10, boys. Our youngest patient was 15 months old at the time of onset, and the disease has been noted by one of us in a person of 69 years.

The economic status and type of home environment have no apparent bearing on the incidence. In our series several of the children came from better than average homes; others lived in shacks and hovels. In every instance, however, there was heavy exposure to dust.

Recent arrival in the region was found to be an outstanding predisposing factor. Of our 24 patients 9 had lived in the San Joaquin Valley less than a year.

PATHOGENESIS

The portal of entry is almost certainly the respiratory tract. The fungus is probably conveyed in dust, and the frequency of cough and sore throat at the onset points to an initial respiratory infection. At or soon after the onset a marked specific sensitivity to the filtrable products of the fungus is established, and it seems highly probable that this plays an important part in producing the symptoms and tissue alterations that occur during the first and second stages of acute coccidioidomycosis, paralleling in these respects the primary infection in tuberculosis. Dickson[10] suggests that the primary infection may, indeed, be in the pulmonary parenchyma, like the foci of Ghon. The fact that spherules can so frequently and with such ease be found in the sputum early in the disease probably indicates that the bronchial mucosa is the seat of extensive infection. On the other hand, the frequency of pleural pain at the onset and the extensive pulmonary shadows found a little later in the x-ray films suggest early pulmonary infection.

As far as we know, the initial attack of coccidioidomycosis with erythema nodosum does not lower the body's defenses against subsequent infection as is supposed by some observers to be the case in tuberculosis. On the contrary, an effective and probably permanent immunity appears to be set up. With rare exceptions, coccidioidal granuloma has not been observed in patients who have had acute coccidioidomycosis with erythema nodosum, and a second case of the latter in the same individual is also extremely rare. The specific sensitization may continue throughout life. We have found it demonstrable 21 years after an attack of erythema nodosum.

PATHOLOGIC ANATOMY

Since no patients are known to have died during or soon after the onset of acute coccidioidomycosis, nothing definite is known of the gross or histologic changes occurring in the human disease at that stage. That they may be similar to the lesions of primary tuberculosis is suggested by the findings of Cox and Smith.[24] In their experimental infections, fibrosis and apparently beginning calcification occurred although organisms remained viable in animals for periods up to two and one-half years. They reported four instances of completely arrested coccidioidal granuloma of the lungs or bronchial lymph glands in patients dying of other causes and examined in the Stanford autopsy service from 1932-1937. Their comments on these lesions are: "In a number of respects they resemble the reaction of the tissues to a primary tuberculous infection: the pulmonary lesions were localized; they were situated peripherally in the lungs without constant relationship to the apices; caseation of the lesions in lymph nodes was prominent in one case, and all lesions showed extensive central caseation with calcification." The

roentgenographic evidence found during the initial stage also suggests a striking similarity in the pathologic lesions in the two diseases.

SYMPTOMS

The acute primary infection with fungus coccidioides has the features of a systemic infection, not unlike influenza, with both upper and lower respiratory manifestations. Because of the general nature of the symptoms at the onset the patient is rarely brought to the physician then or, if he is, the physician usually makes a diagnosis of influenza, pleurisy, or occasionally bronchopneumonia. However, in the San Joaquin fever form of the disease, after an interval during which the patient often feels well, the undiagnosed first stage is followed by a spectacular second stage marked by erythema nodosum and sometimes arthritis and conjunctivitis which brings the patient to the physician and enables him to make the correct diagnosis. This is the classical picture of valley fever seen in nearly all the patients of the present series and in the great majority of primary infections which have been diagnosed up to the present time. That many cases occur without the spectacular second stage or are entirely subclinical can hardly be questioned, since coccidiodin skin tests reveal many positive reactions in apparently normal healthy residents or former residents of the San Joaquin Valley, who have never had erythema nodosum.[23] Other variants occur which will be discussed. Even in the typical valley fever group, the first stage may be mild, moderate, or severe. The second stage, too, may vary in intensity, but on the whole is somewhat more uniform.

A review of our cases has revealed the following picture.

The onset was usually sudden with moderate fever and in most cases a dry cough. Occasionally there was a chill. In about half the cases generalized aching, sore throat, headache and loss of appetite were each noted; and one or more of these in nearly every case. Rarely the children were merely fretful. In more than a third of the cases there was pain in the chest, either unilateral or substernal, which was made worse by deep breathing and was obviously of pleural origin.

These initial symptoms subsided in a week or so, but were occasionally more persistent. In three instances an erythematous rash, generalized or limited to the trunk appeared a few days after the onset. Night sweats also occurred at about the same period in three cases.

At an interval ranging from three to eighteen days with an average of eleven days from the onset, erythema nodosum appeared in 22 of the 24 patients. In all cases but one the lesions appeared on the anterior tibial surfaces and were fairly symmetrical. In many instances they also appeared on the lower anterior surfaces of the thighs, occasionally on the lateral surfaces of the hips, thighs and legs, on the buttocks and on the extensor surfaces of the arms, forearms and elbows. The lesions presented the typical appearance of raised, brightly erythematous, roughly

circular patches, sometimes confluent, tender to pressure, which gradually turned to a purplish and eventually to a brownish color and disappeared in the course of one to three weeks. In a few instances the lesions recurred after a few days or came out in successive crops. During this period fever usually recurred; as a rule it was low, but in one case reached 103.5° F. Simultaneously with the erythema nodosum, signs of acute arthritis were noted in 9 cases, involving the knees and ankles and in 1 case the shoulders. The joints were not red but were tender to pressure, painful on motion, and in one case slightly edematous. Hyperemia of the conjunctiva was also noted at this time in four cases. In one case erythema multiforme appeared at the same time on the forehead, cheeks, and neck.

In two cases in our series, the acute disease ran its course without the development of erythema nodosum or arthritis. We suspect that such an occurrence is much more frequent than the relative incidence in our series would indicate, for it must be remembered that up to the present time the great majority of recognized cases have been brought to medical attention and positively diagnosed because of erythema nodosum. One of these patients, eight days after a rather mild onset, developed purulent pleurisy. Two hundred cubic centimeters of fluid were removed, from which fungus coccidioides was obtained. The patient recovered without operation in about three weeks. He was known to be quite well seven months later. The other patient had a severe onset with symptoms of the usual type, including pleural pain, and developed an erythematous rash on the trunk on the fourth day; the fever and most of the other symptoms disappeared on the seventh day, but the cough persisted another week, and he felt somewhat prostrated for about two months longer.

That subclinical infections or infections with symptoms so mild as to be overlooked or disregarded frequently occur can hardly be questioned.

Physical examination at the onset, even when pleural pains were present, revealed little more than evidences of prostration and fever. The throat was sometimes hyperemic. Most of our information on this period is, however, secondhand, since most of the patients live in rural districts and were not seen by the local physician until a few days or more after the onset. Nearly all of the patients were, however, examined by one of us at or shortly after the emergence of the erythema nodosum, and at that time the only physical abnormalities discovered were the skin manifestations described, hyperemia of the conjunctiva, and signs of arthritis. In view of the changes found repeatedly by x-ray in the chest, the absence of corresponding physical signs is rather striking.

LABORATORY AND OTHER AUXILIARY TESTS

Blood.—In no instance was a blood count taken at or very near the onset or, indeed, before the appearance of erythema nodosum. In one case, a count taken three days after the latter had broken out showed

quite normal total and differential figures, and the red cells and hemoglobin were also normal. In another case, the examination also made three days after the appearance of erythema nodosum showed 20,300 leucocytes, 84 per cent of which were neutrophiles and 16 per cent, lymphocytes; the patient was not apparently feverish or ill at the time, and no later complications developed. Dickson[5] has observed a moderate eosinophilia during the period of erythema nodosum.

The sedimentation rate was determined in two cases, both with the Cutler 50 mm. tube. In one of these the rate two days after erythema nodosum appeared was 31 mm. in one hour; seven days later it was 9 mm.; and six months later, 10 mm. In the other case the rate 11 days after erythema nodosum appeared was 30 mm. in one hour.

Sputum Examination.—In four cases *Coccidioides immitis* was grown from the expectorated sputum and in two others from sputum obtained by gastric lavage. Guinea pigs were inoculated with culture in all these cases and the organism cultivated from the tissues.

Coccidioidin Test.—This was positive in all of our series with one exception; in this the parents refused to have it done and the diagnosis was established by recovery of the organism from the sputum. With the usual amount, 0.1 mg., the reactions ranged in size from 13 to 80 mm. in diameter at forty-eight hours. In the one case where a larger amount (10 mg.) was used the reaction measured 60 by 110 mm. with a large central vesicle.

Tuberculin Tests.—Intracutaneous tuberculin tests, usually with 0.1 mg., were made in 15 of our 24 patients at or about the same time as the coccidioidin tests; they were negative in 13 cases, positive in one and questionable in one.

ROENTGENOGRAMS

Chest films were made from six children soon after the onset of erythema nodosum and revealed similar changes in all. Fuzzy densities were seen at the lung roots, extending for variable distances into the lung fields, in some instances out to the periphery, and having the appearance of consolidation without lobar distribution. The picture was that of bronchopneumonia, indistinguishable from that seen in so-called "epituberculosis." In one instance a small interlobar effusion was found. In the course of a few weeks, the pulmonary densities cleared remarkably. In one case, x-ray studies were made 3 days, 16 days, 2½ months, 5 months, and 2 years after erythema nodosum had appeared. Little change had occurred in the second film, but in the third the density "had cleared out very remarkably leaving only the faintest perceptible granularity." (This was probably due to small deposits of calcium.) In the fourth there was still some fuzzy density at the lung roots and some spots of calcification and in the fifth the picture was about the same. The lung fields were clear in the fourth and fifth films. In another case

films were made 18 and 37 days after erythema nodosum appeared; the first showed heavy root shadows and also a heavy patch of density extending from the lung root to the periphery; 19 days later the pulmonary density had nearly cleared. As yet we have seen no x-ray studies of the chest during the first stage. The pleural pain common at that time suggests that peripheral lesions might already be present.

DIAGNOSIS

In the San Joaquin Valley it is possible to make a presumptive diagnosis of primary coccidioidomycosis on the basis of an attack of fever and cough with one or more of the other onset symptoms such as generalized aching, headache, loss of appetite, sore throat, and pleural pain, followed after an interval of a few days to two and a half weeks by erythema nodosum. For positive diagnosis, however, either a positive skin test or a positive culture from the sputum or both are required. Typical double contoured spherules, with or without endospores, can sometimes be demonstrated in fresh sputum preparations and provide a valuable clue, but they cannot be accepted as conclusive diagnostic evidence without confirmation by culture and animal inoculation.

The routine skin test consists of an intracutaneous injection of 0.1 c.c. of a 1:1000 solution of coccidioidin* (0.1 mg.). The reaction begins to appear in about twelve hours, is well marked at twenty-four hours, and reaches its maximum size and intensity in about forty-eight hours. It is closely similar to the tuberculin reaction, with both erythema and induration and, in some instances, vesiculation.

Sputum or gastric contents should be concentrated by centrifugation and the sediment examined microscopically in the wet preparation without staining for coccidioides spherules. Antiformin should not be used since it kills the fungus, and it is necessary to make cultures. Part of the sediment is planted on Sabouraud's medium and part injected intraperitoneally and intratesticularly into guinea pigs. Before the specimen is considered positive, the fungus should be recovered from the inoculated animal. With intratesticular inoculation, this can be accomplished in ten to thirty days. Primary tuberculosis (of the so-called childhood type) with hypersensitivity to tuberculin is the chief condition from which primary coccidioidomycosis must be differentiated. Both produce an initial fever frequently followed after an interval by erythema nodosum. In coccidioidomycosis the initial symptoms, other than fever, are usually more pronounced than in tuberculosis. The changes found by x-ray in the chest in the two conditions are strikingly similar: In both, extensive infiltrations about the hilum or in the

*Coccidioidin used in this study was prepared by growing four strains of fungus coccidioides on Long's synthetic medium for two months. After Berkefeld filtration, merthiolate was added to a final concentration of 1:10,000. After sterility tests were completed, tests for potency were made on known sensitive individuals. Control tests with the same lots of media incubated for the same period of time have been consistently negative. Considerable variation in potency of different lots of coccidioidin occurs. The stated dosage of 0.1 mg. was that of lots used in this study.

parenchyma out to the pleura are of the same type ("epituberculous infiltration") and clear in the course of a few weeks or months, leaving no trace or sometimes spots of calcification. Rheumatic infection must also be considered as a possibility in the cases with arthritis since erythema nodosum sometimes accompanies that disease. The symptoms at the onset and the x-ray changes may also suggest bronchopneumonia with or without pleurisy. More commonly the symptoms suggest influenza; here the resemblance is quite close, both conditions being accompanied by fever, cough, headache, generalized aching. In any case the diagnosis must depend upon the demonstration of a positive skin test or the recovery of the fungus from the sputum or gastric washings.

PROGNOSIS

The outlook for recovery is, so far as we know, entirely good and, on the evidence thus far accumulated, the danger of ensuing coccidioidal granuloma appears remote. In a combined series of over 700 patients with valley fever only one developed coccidioidal granuloma; in this case, meningitis. Physicians in the region of greatest prevalence unanimously state that they have observed no association. Victims of coccidioidal granuloma rarely exhibit the marked sensitivity to coccidioidin characteristic of valley fever patients even five to twenty-one years after erythema nodosum. The study of the acute disease is, however, comparatively new, and the problem is incompletely solved.

TREATMENT

Treatment consists of bed rest and symptomatic measures during the acute period. No specific method is available. Sedation may be necessary during the onset, or acetylsalicylic acid may be sufficient to relieve the aching and the headache. Cough is sometimes troublesome enough to require a sedative. Protective dressings may be used for a few days to protect the sore shins and joints during the period of erythema nodosum. At this stage, acetylsalicylic acid in large doses or codeine may be needed to relieve pain. In our case with massive pleural exudate, one aspiration only was required, and we know of no case in which operative drainage has been necessary. In cases with pulmonary infiltration it is wise to keep the patient's activities restricted for a few weeks after the temperature has reached normal.

SUMMARY

An acute febrile illness has been described, caused by the fungus *Coccidioides immitis*, characterized by initial systemic symptoms commonly followed by erythema nodosum, and accompanied by a marked specific sensitivity to the products of the fungus. It is common among children. The prognosis, in contrast to that of coccidioidal granuloma which is caused by the same organism, is favorable.

While the endemic focus is in the west, migration of persons in the incubation period could permit the disease to break out sporadically in other localities.

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THE RELATION OF DYSENTERY TO THE ACUTE DIARRHEA OF INFANTS AND CHILDREN

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THE causes of acute diarrhea in early life and of its accompanying symptoms are not always obvious. There is no doubt that many cases are due to infection of different types,[1] and often the organism responsible is the dysentery bacillus. Streptococci may be the cause in isolated cases and sometimes in epidemics, and a form of streptococcus (streptococcus micro-apoikia, gastroenteritidis) was found in an epidemic studied by one of us (Cooper) to fulfil all the usual criteria which would warrant considering it the causative agent.[2] Not so clearly established as etiological agents but occasionally the probable cause of gastroenteric inflammation are other organisms, such as the gas bacillus and the *Salmonella morgani;* and it would appear possible that the colon bacillus might at times take on pathogenic properties.[3] The role of parenteral infections as a cause of gastroenteritis has probably been overemphasized.[4]

There has been raised from time to time the question whether most cases of gastroenteritis in infancy and childhood are not actually caused by the dysentery bacillus. The only means of settling this issue is by careful bacteriologic study since clinical symptoms will not serve to differentiate dysentery from nondysenteric cases. That is to say, no criteria, such as blood and pus in the stools, the degree of toxicity of the patient, the occurrence of dehydration or acidosis, the severity and length of diarrhea, or the case mortality, are of final value in determining that an individual case is or is not due to dysentery infection. In this report we shall term "dysentery" those cases of acute diarrhea in infants and children in which any organism of the Shigella group (dysentery bacilli) was recovered, and "nondysentery" those in which it could not be recovered.

The varying incidence of dysentery infection which has been reported is influenced by persistence in the search for the organism, by the locality in which the disease occurs, and, as will be shown in this report, by the age of the patient. The incidence of positive cultures for dysentery from

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The statistical analyses were made by Estelle W. Brown, statistician of the Children's Hospital Research Foundation.

the stools of infants and children suffering from gastroenteritis is influenced also by the conditions in the epidemic: for example, in Cincinnati we found it to vary over a period of years from 21 to 36 per cent; during this period similar measures of study were employed.

In the attempt to answer the specific question of how much gastroenteritis was actually caused by dysentery infection, we undertook an extensive study during the summer of 1938. Two hundred and nine infants and children suffering from acute diarrhea were admitted to the Children's Hospital of Cincinnati or to the Pediatric Wards of the Cincinnati General Hospital. By special arrangement and nursing care, by messenger service, and by cooperation in the laboratory, stools were obtained and received in the laboratory usually within 30 minutes after being passed, and cultures were immediately started. From 745 stools of these 209 patients cultures were made on 11,530 plates of media. From the stools of 101 of these patients were recovered dysentery organisms of one or another type. The incidence of dysentery, therefore, in this group of children was 49 (48.8) per cent. A total of 379 stools (3.8 stools per patient) were examined from the dysentery group and 366 (3.4 stools per patient) from the nondysentery group. In one patient, who died before a stool could be obtained, dysentery organisms were found in the gastroenteric tract at autopsy; thus there were 102 patients in the dysentery group as compared with 107 patients in the nondysentery group. Cultures of 8 patients, obtained from the gastroenteric tract at autopsy, served to corroborate the diagnosis made from stool culture before death. Nine patients were admitted more than once during the period of this study: 4 of these had positive stool cultures on two admissions, 4 had negative stool cultures on the first admission but positive on the second, and 1 had positive stools on the first two admissions but negative on the third. In these instances each patient was included only once in the analysis.

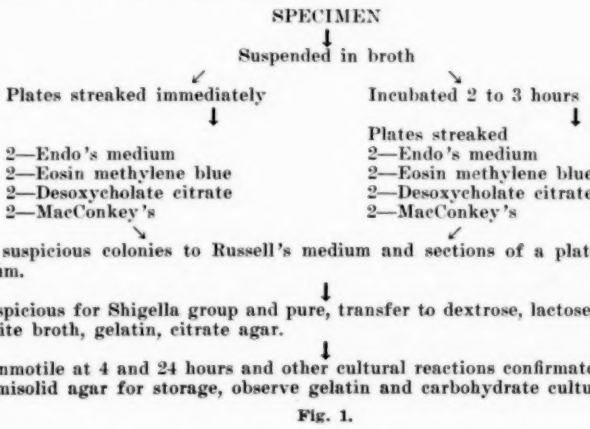
SPECIMEN
Suspended in broth
Plates streaked immediately
2—Endo's medium
2—Eosin methylene blue
2—Desoxycholate citrate
2—MacConkey's
Incubated 2 to 3 hours
Plates streaked
2—Endo's medium
2—Eosin methylene blue
2—Desoxycholate citrate
2—MacConkey's
Pick suspicious colonies to Russell's medium and sections of a plate of Endo's medium.
If suspicious for Shigella group and pure, transfer to dextrose, lactose, saccharose, mannite broth, gelatin, citrate agar.
If nonmotile at 4 and 24 hours and other cultural reactions confirmatory, transfer to semisolid agar for storage, observe gelatin and carbohydrate cultures 30 days.

Fig. 1.

Fig. 1 gives in outline form the method of bacteriologic study. Briefly, a specimen of each stool was suspended in broth and immediately streaked on eight plates; the broth suspension was then incubated for two or three hours and streaked on eight additional plates. In both cases these eight plates consisted of two each of the following media: Endo's, eosine methylene blue, sodium desoxycholate citrate,[5] and MacConkey's.* After incubation overnight several colonies, suspicious for dysentery bacilli, were picked and transferred to sections of plates of Endo's medium and to tubes of Russell's medium. After incubation of 12 to 18 hours the Russell's medium was observed, and, if the cultural reaction consistent with the Shigella group was present, it was considered as partially confirmatory. The colonies on the Endo's medium were then observed, and, if pure, they were transferred to dextrose, lactose, saccharose, mannite and dulcite broth, also to plain broth for motility observation at 6 and 24 hours; to litmus milk, gelatin, citrate medium, and nitrate broth. If the cultural reactions observed in these media were those expected for dysentery bacilli, a transplant was made into semisolid agar medium for storage of the culture. The carbohydrate and gelatin cultures were observed for 30 days. Difco dehydrated medium was used throughout, except for the sodium desoxycholate citrate medium which was obtained from the Baltimore Biological Laboratories. At the time of this report most of the cultures which have been saved in semisolid agar medium have been restudied in the same manner as before; in addition on the following carbohydrate media: sorbitol, salicin, inosite, raffinose, rhamnose, xylose, mannose, and levulose. These carbohydrate cultures have been observed for at least six weeks.

RESULTS

Percentage of Dysentery.—From 102 patients dysentery organisms were recovered. In 107 patients no dysentery organisms were found. The incidence of dysentery, therefore, in this group of 209 infants and children was at least 49 (48.8) per cent.

Fatality Rate.—The case fatality rate was not significantly different in the two groups, being 12.7 per cent (13 of 102 cases) in the dysentery group and 15.9 per cent (17 of 107 cases) in the nondysentery group.

Seasonal Incidence.—In Table I it is shown that the two forms of diarrhea follow the same pattern in seasonal incidence.

Duration.—In Table II is shown the duration of dysentery and nondysentery cases from the time of admission to the hospital to discharge or death. It appears from the figures that the dysentery cases had a slightly longer course than the nondysentery ones. On the other hand, in patients with dysentery who did not recover, the mean day on which death occurred was earlier as compared with the day on which death occurred in the nondysentery patients.

*Formula of January, 1938.

Age of the Patient at Onset of Acute Diarrhea.—In Fig. 2 is shown the frequency distribution of the incidence of dysentery and nondysentery cases according to the age of the patient at the onset of acute diarrhea; the mean age in the dysentery group was 26.5 months and in the nondysentery group 11.0 months. In spite of the great variability within both groups, the difference between the two means is a highly significant one. When they are compared by the method of Fisher,[6] p is

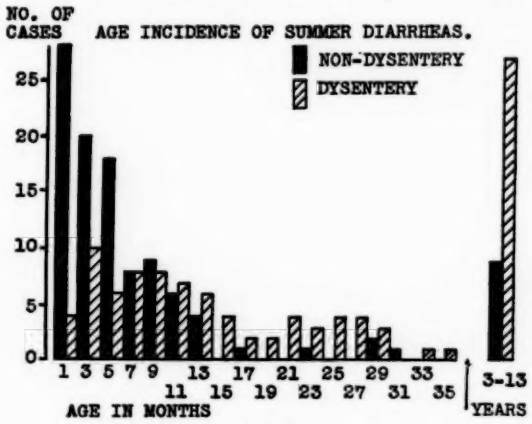

Fig. 2.

found to be less than 0.001. This indicates that a difference as large or larger than that observed would arise by chance alone less often than once in every thousand trials. Values of p of 0.05 or less are accepted as indicating a difference which may be considered significant; that is, a p of 0.05 indicates a 5 per cent chance of this difference occurring by chance alone.

Table I

Seasonal Incidence of Summer Diarrhea

Month	Number of Cases		
	Dysentery	Non-dysentery	Total by month
May	1	2	3
June	16	18	34
July	32	36	68
August	33	36	69
September	20	15	35
Total	102	107	209

Table II

Duration of Summer Diarrhea

	Dysentery		Non-dysentery	
	Mean in days	S.D. ±	Mean in days	S.D. ±
Total cases	30.0 ± 1.7	17.0 ± 1.2	24.3 ± 1.4	14.4 ± 1.0
Recovered	36.1 ± 1.5	13.0 ± 1.1	24.8 ± 1.5	14.0 ± 1.1
Died	17.2 ± 3.4	12.2 ± 2.4	21.8 ± 3.9	16.3 ± 2.8

These data also indicate that, at least for the year in which our study was made, acute diarrhea in early infancy was usually not due to dysentery but that in children one year of age or older three-quarters of the cases were caused by the dysentery bacillus. It would suggest further that the percentage of dysentery reported in any study would be influenced by the age distribution of the children involved.

Duration of Disease at Time of Stool Culture.—It is evident in Table III that the duration of the disease at the time when stools were cultured

TABLE III

DURATION OF DISEASE AT TIME OF CULTURE

DAYS AFTER ONSET	DYSENTERY PATIENTS 1ST CULT.	1ST POS. CULT.	NON-DYS. PTS. 1ST CULT.
0	1	1	0
1	18	17	12
2	13	13	5
3	8	7	10
4	14	15	13
5	8	6	11
6	5	5	8
7	8	8	7
0- 7	75	72	66
8-14	15	15	27
15-21	7	9	7
Over 21	4	5	5
Total*	101	101	105
Mean days ± S.E.	6.2 ± 0.6	6.9 ± 0.6	8.3 ± 1.1
S.D. ± S.E.	6.2 ± 0.4	5.6 ± 0.4	11.7 ± 0.8

*Onset date unknown for 3 patients.

in the dysentery group as compared with this factor in the nondysentery group is not significantly different. The mean day in the dysentery group at the time the first culture was taken was 6.2, whereas in the nondysentery group it was 8.3. The mean day on which the first positive culture was obtained in the dysentery group was 6.9. The standard deviations indicate that the variation within each group was so great that this difference cannot be considered more than a chance phenomenon.

Further information concerning the value of early cultures is given in Table IV, in which is recorded the prevalence of positive dysentery stools arranged according to the duration of the disease.

Evaluation of Different Culture Techniques.—Some of the data obtained may be analyzed from the standpoint of the efficiency of the various culture media. Table V gives the basic data on the number of stools studied per patient. Fig. 3 demonstrates the results which were obtained by culturing a varying number of stools from the 101 patients on four media. The first histogram of this figure shows the number of

TABLE IV

RELATION OF POSITIVENESS OF STOOLS TO DURATION OF DYSENTERY

DAYS AFTER ONSET	NO. OF STOOLS CULTURED	POSITIVE %
1	37*	97
2	40	95
3	35	94
4	40	90
5	42	76
6	25	76
7	21	81
	—	—
0- 7	240	88
8-14	79	67
15-21	33	64
Over 21	27	44
	—	—
Total	379	78

*Includes one stool taken day of onset.

patients in which dysentery bacilli were found positive when the first stool was cultured on each medium: 54 on Endo's, 65 on eosine methylene blue, 73 on MacConkey's and 82 on desoxycholate citrate. In 88 patients the first stool was found positive when all four media were used (see last histogram of Fig. 3).

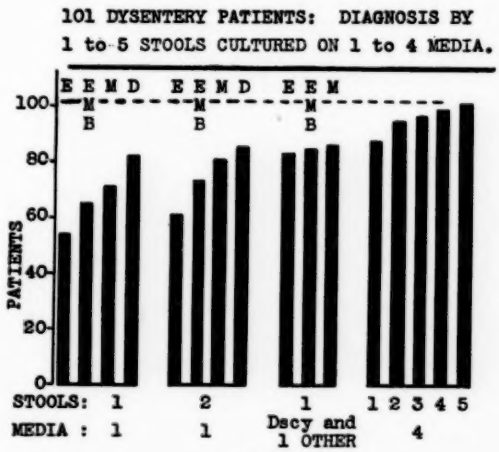
101 DYSENTERY PATIENTS: DIAGNOSIS BY
1 to 5 STOOLS CULTURED ON 1 to 4 MEDIA.
E E M D E E M D E E M
M M M
B B B
100
80
60
40
20
0
PATIENTS
STOOLS: 1 2 1 1 2 3 4 5
MEDIA : 1 1 Dscy and 1 OTHER 4

Fig. 3.

The second histogram of Fig. 3 shows the number of patients found positive for dysentery when two stools were cultured on each medium. The results are not strikingly different from those when one stool is cultured. That is, with the best medium, desoxycholate citrate, the number of cases in the dysentery group was increased from 82 to 85. Since

desoxycholate citrate appears to be the best of the four media, there is presented in the third histogram of Fig. 3 the results obtained when desoxycholate citrate and one other medium are used for culturing one stool. It is seen that, whereas the use of desoxycholate citrate alone resulted in 82 positive diagnoses (see first histogram), desoxycholate citrate used in combination with Endo's medium resulted in 83 positive diagnoses, desoxycholate citrate with eosine methylene blue medium in 85, and desoxycholate citrate with MacConkey's medium in 86. That is, the maximum gain was with MacConkey's medium which added only 4 more cases to the dysentery group than when desoxycholate citrate alone was used on one stool.

TABLE V

STOOLS FROM ALL PATIENTS

NO. STOOLS STUDIED	DYSENTERY GROUP		NONDYSENTERY GROUP	
	NO. PATIENTS	NO. STOOLS	NO. PATIENTS	NO. STOOLS
1	23	23	36	36
2	6	12	10	20
3	7	21	9	27
4	4	16	1	4
5	59	295	42	210
6	2	12	4	24
7			1	7
8			1	8
10			3	30
Total	101	379	107	366

It is obvious that it would be possible to combine the media and the number of stools in many ways, but for this presentation it appears to be sufficient to show the optimum results when all four media are used to study from one to five stools. It is seen in the last histogram of Fig. 3 that 7 cases which had been found negative by culturing the first stool were positive on the second, and that two more positive cases were added by studying each of the three succeeding stools. For each procedure the total number of positive cases would have been found without the use of Endo's medium, but the greatest number of positive cases were found with the use of the other three media. From this it would appear that Endo's medium could safely be eliminated in further studies. It would also appear that the number of stools to be cultured and the number of media to be employed must be decided by the degree of accuracy needed for the study. It is obvious, however, that a single negative stool culture is not proof that dysentery organisms are absent. In discussing the value of the different media, it must be borne in mind that part, at least, of the increased efficiency of the several media may be due to the increased sampling from a given stool culture. This possibility suggests the desirability of further study to develop a technique which will secure a more homogenous sampling of the stool.

TABLE VI

DISTRIBUTION OF POSITIVE PLATES BY MEDIA AND METHOD

STOOL NO.	ENDO		E. M. B.		MAC C.		DSCY.		TOTAL
	DIRECT	INCUB.	DIRECT	INCUB.	DIRECT	INCUB.	DIRECT	INCUB.	
1	39	23	45	34	51	43	67	62	364
2	35	27	32	38	42	37	59	54	324
3	21	18	31	27	33	33	51	52	266
4	27	20	32	25	32	35	50	51	271
5	24	27	35	30	29	35	44	42	266
Total	146	115	175	154	187	182	271	261	1491
Pos.	28%		36%		40%		58%		

TABLE VII

TOTAL POSITIVE PLATES FOR MEDIA AND METHOD

DAYS AFTER ONSET	STOOL NO.	ENDO	E. M. B.	MAC C.	DSCY.	TOTAL	DIRECT	INCUBATED
6.3	1	62	79	94	129	364	202	162
7.0	2	62	70	79	113	324	168	156
7.8	3	39	58	66	103	266	136	130
8.5	4	47	57	66	101	271	141	130
9.8	5	51	65	64	86	266	132	134
Total		261	329	369	532	1491		

ANALYSIS OF VARIANCE

VARIANCE	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	S. D.
Between stools	4	976.1	244.0	15.62
Between media	3	3977.7	1325.9	36.41
Betw. dir. and incub. plates	20	409.5	20.5	4.52
Interaction	12	218.7	18.2	4.27
Total	39	5582.0		

Efficacy of the Four Media.—A much more exact analysis of the efficacy of the various media may be made from a study of those 46 cases in each of which cultures from 5 stools were made on four plates with each of the four media; that is, 16 plates per stool and a total for the 46 patients of 230 stools and 3,680 plates. The number of positive plates from each stool and from both the direct culture of the stools and from the incubated broth suspension of the stools on each medium are noted in Table VI. The total number of positive plates from the first, second, third, fourth, and fifth stools, respectively, appear in the right-hand column, and the total for each medium and method in the next to bottom row. It is apparent that on the desoxycholate citrate medium the direct and the incubation methods gave almost identical results, and that on the other three media there appeared to be a slight advantage in the

direct method. The total efficiency for each medium (direct and indirect methods on all stools) is expressed in percentage (bottom row) of the 920 plates of each medium. In order to evaluate more critically the relative importance of the main variables, these same data are arranged for analysis of variance in Table VII.

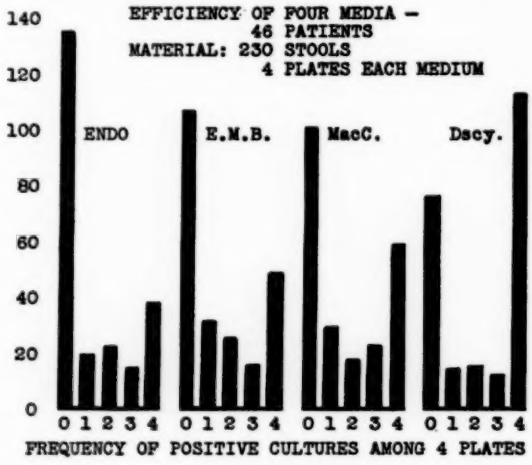

Fig. 4.

Analysis of Variance.—The factors which are of most importance in this analysis are the variation in the response between the different types of media with the same stool and the irregularity in response of the same medium with different stools. The method of culture is of much less importance; since the direct method is a shorter procedure and in most cases has a slight advantage over the method by incubation, it would appear that it could be recommended. The final factor of interaction or the selective action of the different media for different stools also contributes to the variance, but in general the four media behave in a similar manner for each succeeding stool.

The efficacy of the four media may be examined from a different point of view. When four plates are streaked from the same sample of stool from a known case of dysentery, five possibilities arise. All four plates may be negative; one may be positive and three negative; two may be positive and two negative; one may be negative and three positive; or finally all four may be positive. Obviously, the use of the medium which secures the most positive cultures in all plates will be the most efficient and on that medium it is justifiable to streak fewer plates, since if all four were positive one would do as well as four. The frequency with which these five possibilities occurred for each of the four media is shown in Fig. 4.

It is apparent that desoxycholate citrate was far superior to any of the other three media,* that there was little to choose between eosine methylene blue medium and MacConkey's medium, and that with Endo's medium there were more negative cultures on all four plates than positive in all four.

Even though the desoxycholate citrate medium is much better than the other media, one must recognize that the efficiency of the culture technique is alarmingly low since only 58 per cent of the 920 plates with this medium were positive. How many of the negative plates were due to variation in stools or in sampling cannot be estimated, but the fact remains that there is need for further study of stool culture technique. Since it is apparent that the number of positive plates decreases as the disease progresses, it would seem wise to use more plates on more stools for patients who are to be examined relatively late in the disease.

This analysis also suggests that any report of the incidence of dysentery in any given community or epidemic of acute diarrhea which has relied upon examination of stools with Endo's medium alone must be re-evaluated upon the basis of these findings.

Identity of Dysentery Organism.—The organisms of the 102 patients with positive dysentery cultures were grouped on the basis of their cultural characteristics. Thirty-seven of the patients had organisms of the Sonne type, 59 of the Flexner type and 6 had dulcite fermenters.

For 95 patients the recovered dysentery organisms were tested with 4 previously prepared antisera. Of these 76 agglutinated significantly.

Details of the fermentative and serologic studies will be reported later.

SUMMARY

An intensive study on the stools of infants and children suffering from acute diarrhea was carried out on 209 patients during the summer of 1938.

From 102 patients (49 per cent) dysentery organisms were recovered.

The seasonal incidence, case fatality rate and duration of gastroenteritis were not significantly different in the dysentery and nondysentery groups.

The frequency distribution of the two groups according to the age of the patient was strikingly different. Seventy-five per cent of the patients under 1 year of age did not have dysentery while 75 per cent of those over 1 year did.

The data have been analyzed statistically from the standpoint of the efficiency of several culture media used. Sodium desoxycholate citrate medium is markedly superior for isolating dysentery organisms.

The type distribution of the dysentery organisms is given.

*This conclusion is in agreement with the recent report of Hardy and his colleagues.[1] The use of this medium was suggested to us by Dr. Hardy.

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VITAMIN A ABSORPTION IN CELIAC DISEASE

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IN 1934 Chesney and McCoord[1] reported observations on the absorption of vitamin A from the intestine in 2 cases of celiac disease and in 12 cases without celiac disease. This report deals with the results of the test in 10 cases of celiac disease, one case of suspected cystic fibrosis of the pancreas, and in 48 cases with other complaints.

The vitamin A content of the blood is determined by the method of Carr and Price with some modification by McCoord and Clausen.*[2] This colorimetric determination may be carried out in any well-equipped laboratory, but great care must be used in the preparation of the reagents, and the speed necessary for carrying out the test must be acquired by practice. The determination of the carotinoids or plant pigments; xanthophyll, and carotene, which is necessary for correction of the vitamin A results, is made by the method of Clausen and McCoord.[3]

The procedure used for testing the absorption of vitamin A is that of Chesney and McCoord.[1] After a basal blood specimen is taken, the child is given orally an amount of fish liver oil† which furnishes 7000 U. S. P. units per kilogram of body weight. Blood specimens are taken at 2, 4, 6, 9, 12, and 24 hours after the administration of the oil. During the test the child receives his regular meals except that cod liver oil and vitamin A concentrates are omitted from the diet.

The results of the individual tests are recorded in Tables I and II. The means, medians, and standard deviations with their probable errors are found in Table III and the graphic presentation in Chart 1.

It is clear that the patient with celiac disease, even after treatment, is unable to absorb vitamin A as well as most patients without celiac disease. Although our series of cases of celiac disease is relatively small, this finding is so constant that we feel it is significant. In the one case of suspected cystic fibrosis of the pancreas (Case 66) the patient was unable to absorb vitamin A.

In the control group the majority of patients showed the greatest amount of vitamin A in the blood at the end of four hours. However, there was considerable variation in the time of appearance of the maximum level as well as in the amount of vitamin A found in the blood

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*All results are given in "blue units" of vitamin A. This is an arbitrary unit roughly equivalent to between 3.5 and 4 U. S. P. units. Using a 10 per cent solution of copper sulfate as a standard, serum of sufficient content of vitamin A to match the standard when acted upon by an antimony trichloride reagent is considered to contain 100 blue units of vitamin A per 100 ml. Corrections are made for xanthophyll and carotene content of the blood.

†The oil used in these tests has been supplied to us through the kindness of Dr. Carl Neilson of the Abbott Laboratories. The oil used at present contains 210,000 U. S. P. units per gram.

TABLE I

DATA ON CASES WITHOUT CELIAC DISEASE

CASE NO.	AGE YR.	SEX	VITAMIN A ABSORPTION IN UNITS VITAMIN A PER 100 C.C. OF BLOOD								TOTAL PLANT PIGMENT IN γ	RISE GLUCOSE TOLERANCE MG. %	% FAT DRY WT. STOOL	DIAGNOSIS
			HOURS											
			FASTING	2	4	6	8	9	12	24				
1	10	F	24	28	42	59	--	40	28	32	155	64	--	Abdominal pain, ? etiology
2	10	M	35	59	135	110	--	62	46	23	80	--	--	Influenza
3	9	M	5	8	182	62	--	38	40	38	--	49	22	Malnutrition
4	3	M	23	91	102	--	312	--	132	38	420	60	21	Feeding problem
5	11	F	25	40	137	140	--	69	59	42	142	--	--	Dermatitis (contact)
6	4	M	19	--	200	--	--	66	--	--	172	35	24	Secondary anemia
7	6	M	5	30	198	109	--	81	76	20	90	--	--	Catarrhal jaundice (3rd day)
8	10	F	17	37	270	81	--	50	51	34	116	--	--	Chorea
9	4	F	23	103	223	145	--	70	65	27	220	162	--	Acondroplastic dwarfism
10	8	F	22	50	200	300	--	92	62	73	76	--	--	Orthostatic albuminuria
11	4	M	10	46	106	94	--	--	--	42	--	26	30	Cervical adenitis
12	12	M	5	8	80	172	--	97	50	12	184	--	--	Catarrhal jaundice (6th day)
13	3	M	10	53	270	125	--	40	37	20	77	70	47	Constipation
14	8	M	12	26	400	328	--	84	51	30	--	41	--	Epilepsy
15	2	M	17	26	63	112	--	96	--	19	224	113	48	Secondary anemia
16	6	M	25	38	--	138	--	88	64	24	--	61	19	Pituitary dwarfism
17	13	F	50	108	178	105	--	88	73	48	304	--	42	Diabetes mellitus
18	13	M	12	9	27	210	--	144	65	30	112	16	--	Epilepsy
19	32	M	12	65	93	64	--	65	--	85	--	53	--	Psychosis
20	8	M	2	4	3	5	--	--	--	2	112	--	--	Catarrhal jaundice (10th day)
20	8	M	21	20	76	117	--	274	--	47	--	--	--	Catarrhal jaundice (18th day)
21	11	M	13	12	15	10	--	14	13	13	67	5	30	Abdominal pain, ? cause
22	11	M	18	110	263	179	--	70	80	20	72	40	--	Arthritis
23	5	M	23	23	80	100	--	65	--	40	--	51	--	Amyotonia congenita
24	½	F	13	33	50	34	--	23	10	11	--	--	59	Pyuria (40th day)
24	½	F	35	200	216	92	--	72	38	23	--	--	--	Pyuria (51st day)
25	8	M	29	163	100	68	--	--	50	58	110	--	--	Pneumonia
26	10	M	20	20	30	--	58	--	--	16	--	86	22	Vomiting, ? cause

TABLE I—CONT'D

27	9	M	9	100	165	88	--	67	23	21	90	--	--	Catarrhal jaundice (20th day)
28	7	F	32	161	232	140	--	75	49	38	57	--	--	Pneumonia
29	12	M	11	63	128	63	--	67	35	18	188	--	--	Muscular dystrophy
30	2	M	32	476	440	--	--	--	194	55	--	--	--	Malnutrition
31	3	M	48	73	294	275	--	75	69	31	350	22	--	Diarrhea
32	48	M	16	73	363	--	--	187	129	46	180	22	--	Alcoholic neuritis
33	¾	M	31	--	76	--	37	--	--	--	45	25	36	Secondary anemia, rickets and scurvy
33	¾	M	16	40	169	139	--	47	30	18	--	--	51	Secondary anemia, rickets and scurvy
34	12	F	15	45	--	183	--	110	85	--	141	--	--	Catarrhal jaundice (9th day)
35	2	M	28	--	300	--	--	--	49	--	94	23	35	Acute upper respiratory infection,
36	12	M	9	14	29	575	--	285	115	30	112	130	--	Catarrhal jaundice (7th day)
37	2	F	64	187	398	308	--	225	158	37	--	47	41	Measles
38	8	F	25	41	210	120	--	75	51	--	140	--	--	Chorea
39	10	M	21	120	300	145	--	73	62	46	--	59	--	Malnutrition
40	10	M	8	24	182	703	--	126	126	30	128	69	--	Rheumatic fever
41	6	M	8	9	7	43	--	35	60	30	123	49	--	Muscular dystrophy
42	9	F	20	56	132	--	--	--	35	--	--	54	--	? Rheumatic fever
43	4	M	8	15	13	45	--	141	53	15	--	67	33	Varicella, malnutrition
44	½	M	10	12	77	69	35	--	--	--	34	42	36	Pneumonia, secondary anemia
45	3	F	6	41	267	122	--	--	41	29	133	--	--	Pneumonia
46	7	M	7	10	246	222	--	--	88	26	148	103	--	Pituitary dwarfism
47	5	M	12	--	995	355	--	--	107	--	133	15	--	Hypothyroidism
58	5	F	14	38	144	64	--	--	38	15	209	5	--	Alopecia
59	9	M	14	69	69	92	--	41	16	10	--	21	--	Lymphoma
60	11	M	18	14	62	154	--	41	--	19	--	105	20	Tuberous sclerosis
61	11	M	13	147	260	--	132	--	80	20	--	52	--	Hypothyroidism
62	2	M	8	12	74	33	--	25	27	15	--	29	35	Malnutrition
62	2	M		98	115	87	--	--	--	--	--	--	--	Malnutrition (bile given)
63	6	M	10	--	165	55	--	--	22	15	--	--	--	Eczema, asthma
64	13	M	8	21	35	16	--	60	--	48	--	15	--	Scleroderma
65	50	M	18	27	127	41	--	--	--	31	--	--	--	Hypoproteinemia

TABLE II

DATA ON 10 CASES OF CELIAC DISEASE AND ONE CASE OF CYSTIC FIBROSIS OF THE PANCREAS

CASE NO.	AGE YR.	SEX	VITAMIN A ABSORPTION IN UNITS VITAMIN A PER 100 C.C. OF BLOOD — HOURS								TOTAL PLANT PIGMENT IN γ	RISE GLUCOSE TOLERANCE MG. %	% FAT DRY WT. STOOL	REMARKS
			FASTING	2	4	6	8	9	12	24				
48	14	M	12	10	10	--	--	20	--	16	0	4	57	Celiac disease
			11	12	42	42	--	--	13	11		8	52	
			12	12	23	42	--	25	--	13		4	32	
49	7	M	6	9	8	11	--	--	--	5	32	2	33	Celiac disease (raw pancreas given on second determination)
			30	54	34	64	--	40	--	28	73	43	23	
			19	--	19	30	--	--	--	--		25	49	
			18	19	28	23	--	--	--	--		32	30	
50	48	F	9	11	15	31	--	25	32	19	54	11	57	Celiac disease, tuberculosis, peritonitis
51	1½	M	13	12	14	15	--	14	15	16	0	0	41	Celiac disease
52	4	M	13	28	92	78	--	--	39	20	42	54	34	Celiac disease
			21	24	25	43	--	--	85	37	109		16*	*Mean of 4
53	43	M	4	7	6	14	--	8	15	9	81	24	58	Celiac disease
54	4	F	8	11	8	12	--	11	15	14	10	30	46	Celiac disease
			30	21	20	28	--	39	--	19	73	32*	47	*Mean of 3
			10	7	9	18	--	24	--	18	36	35	38	
			28	--	21	45	--	--	37	--	74	15	19	
			16	--	35	--	--	--	--	--	59	57	27	
			17	15	21	30	--	60	--	--	34	32	19	
			17	10	20	12	--	13	10	7	70	12	12	
			11	--	14	10	--	16	--	13	34	47	12	
			7	23	34	33	--	30	33	18	63	19	21	
			11	11	8	13	--	--	10	10	56	17	31	
			8	8	11	8	--	7	7	7		19	25	
55	5	F	3	11	9	16	--	11	--	--	55	21	39	Celiac disease
56	11	F	12	20	37	45	--	80	74	39	31	0	59	Celiac disease
			14	14	100	146	--	52	30	22	126	24	24	
			16	15	11	12	--	13	--	13	109	35	30	
			20	29	58	39	--	39	26	24	84	56	16	
			19	20	28	24	--	18	19	19		30	35*	*Mean of 3
57	11	M	9	14	9	12	--	9	12	13	84	32	41	Celiac disease
			15	15	14	14	--	15	15	10	69	22	36	
			9	16	37	31	--	38	--	--	66		39	
													28*	*Mean of 5
66	1¼	M	5	4	2	8	--	--	--	--	40	63	41	? Cystic fibrosis of pancreas

TABLE III

VITAMIN A CURVES IN NONCELIAC AND IN CELIAC DISEASE

(FIGURES IN UNITS VITAMIN A PER 100 C.C. BLOOD)

TIME	VITAMIN A ABSORPTION NONCELIAC				VITAMIN A ABSORPTION CELIAC				DIFF. MEANS & P. E.
	NUMBER OBSERVATIONS	MEAN AND P. E.	STANDARD DEVIATION AND P. E.	MEDIAN AND P. E.	NUMBER OBSERVATIONS	MEAN AND P. E.	STANDARD DEVIATION AND P. E.	MEDIAN AND P. E.	
Fasting	58	17.5±1.1	12.1±0.7	15.7±1.3	31	13.8±0.8	6.4±0.9	13.2±1.0	3.7±1.4
2 hours	53	60.1±6.7	72.3±1.6	39.8±8.4	27	15.8±1.2	9.1±0.8	13.4±1.5	44.3±6.8
4 hours	55	175.5±14.2	154.0±1.0	150.0±17.7	32	24.7±2.6	21.9±1.8	18.9±3.2	150.8±14.7
6 hours	47	145.5±13.3	135.3±9.4	110.8±16.6	30	28.3±2.8	29.6±2.0	24.0±3.6	117.2±13.6
9 hours	40	83.4±6.4	62.4±4.6	66.5±8.0	23	25.0±3.1	17.0±2.0	19.4±3.9	58.3±7.1
12 hours	45	63.6±5.2	40.0±3.6	54.8±6.6	18	25.0±3.2	22.6±2.2	18.6±4.0	38.6±6.1
24 hours	49	29.1±2.3	15.5±1.6	26.5±2.9	26	16.1±1.8	14.2±1.3	15.0±2.2	13.0±2.9

of different patients. This variation is, in units of vitamin A, much more marked in the nonceliac group than in the celiac group. Relatively, however, as measured by the coefficient of variation, it is about the same in both groups. Taking the four-hour determination, the coefficient of variation is 89 per cent in the celiac group and 88 per cent in the control group.

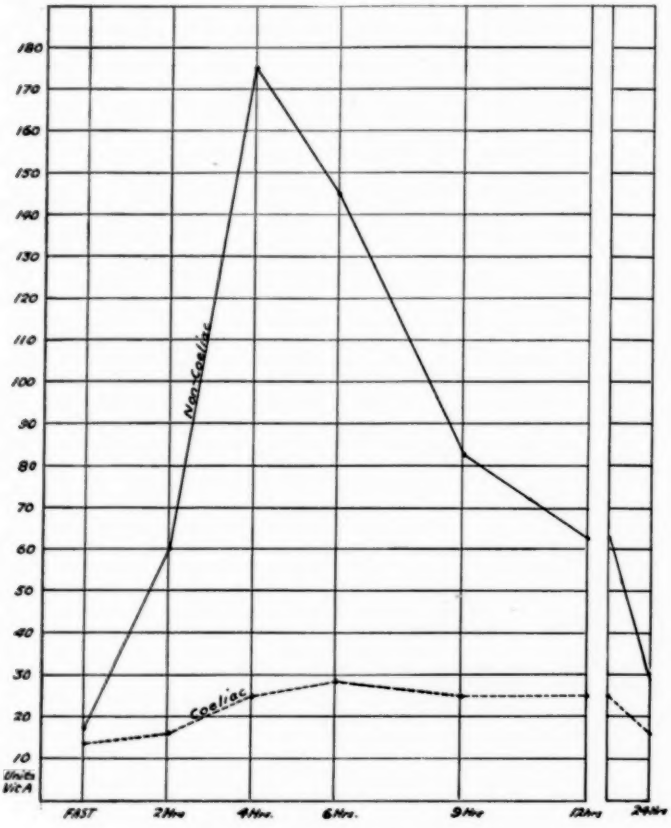

Chart 1.—Vitamin A absorption curve.

The fasting level of vitamin A is also lower in the celiac group than in the controls, but this difference is not statistically significant. Associated with the inability to absorb vitamin A is a lowered concentration of total plant pigments in the blood in the former group (Table IV).

In the normal test, we consider that the vitamin A content of the blood should rise above 100 units of vitamin A at some time during the test. With the exception of one single determination (in Case 56), in no case of celiac disease was there a rise above this level, whereas values

TABLE IV

DISTRIBUTION OF VALUES OF PLANT PIGMENTS IN CELIAC AND NONCELIAC PATIENTS IN WHOM VITAMIN A ABSORPTION CURVES WERE DETERMINED

TOTAL PLANT PIGMENT GAMMA PER 100 ML.	CELIAC DISEASE	NONCELIAC DISEASE	DIFFERENCE OF MEANS AND P. E. OF DIFFERENCE
0-25	3	0	
26-50	6	2	
51-75	9	4	
76-100	5	6	
101-125	2	6	
126-150	1	7	
151-175	0	2	
176-200	0	3	
201-225	0	3	
226-250	0	0	
251-275	0	0	
276-300	0	0	
301-325	0	1	
326-350	0	1	
351-375	0	0	
376-400	0	0	
401-425	0	1	
Total	26	36	
Mean and Standard Error of Mean	58.7±2.2	168.0±13.4	109.2±13.6
Standard Deviation and Standard Error of Standard Deviation	11.3±1.6	80.8± 9.5	
Median and Standard Error of Median	61.2±2.7	128.6±16.9	67.4±17.1

for most of the control group rose well above this level. The exceptions require some comment. In the first place, it is possible that a few patients in both groups did go over this level, but because there were at least two hours between determinations, and sometimes more, the higher levels in the blood were missed. If we take the 100 unit level, there were 11 determinations in the control group which did not rise that high at any time during the test. (Cases 1, 20, 21, 24, 26, 33, 41, 44, 59, 62, and 64.) In four of these cases (20, 24, 33, and 62) a repetition of the test showed that the patient had recovered normal power to absorb vitamin A. In the other cases no second test was done.

CASE 1.—A 10-year-old girl with abdominal pain of undetermined origin had a flat curve. However, the oil with which the test was done was found to have lost its potency.

CASE 21.—This 11-year-old boy had, in addition to the inability to absorb vitamin A, a low or flat sugar tolerance test and a somewhat high level of fat in the stools. Although his chief complaint was pain in the abdomen, his history suggested rheumatic fever or an allergic reaction to food. No definite diagnosis was made. He was to return for further study but failed to appear. He may well have had a mild case of celiac disease. His laboratory findings suggested this.

CASE 26.—This 10-year-old boy came to the hospital with a history of attacks of vomiting and abdominal pain which had been present since infancy. He was found to have a large atonic stomach possibly with a diverticulum near the cardiac end of the stomach. He improved on a Sippy regime. His glucose tolerance test was normal, and apparently the child did not have celiac disease.

CASE 41.—This 6-year-old boy had muscular dystrophy. His vitamin A curve was almost flat, but his blood carotenoids, glucose tolerance, and stool fat were within normal limits. Another child with muscular dystrophy (Case 29) had a normal vitamin A absorption curve, so that this condition is not necessarily associated with lack of ability to absorb vitamin A.

CASE 44.—This 5-month-old infant had pertussis and developed pneumonia, otitis media, and secondary anemia. His plant pigments were low, his stool fat relatively high, but his glucose absorption was normal. He apparently did not have celiac disease.

CASE 59.—This 9-year-old boy, who died, was found to have a plastic peritonitis and fatty degeneration of the liver. He also had a relatively flat sugar tolerance curve but had no other evidence of celiac disease.

CASE 64.—This 13-year-old boy had scleroderma. His glucose tolerance test was normal.

In two other cases, which were so recently studied that they were not included in the tables, failure to absorb vitamin A occurred although neither child had celiac disease. One of these cases was in a 17-month-old infant with partial congenital obstruction of the jejunum resulting in emaciation, failure to gain, and almost constant vomiting. Possibly she vomited bile, or the glucose and vitamin A were caught in a pouch and vomited before they could be absorbed. The obstruction was relieved surgically, and the absorption test will be repeated. The other case is one of an obscure type of hepatitis, chronic in nature, in a girl of 11 years. The child is jaundiced, and liver function tests show that the liver is badly damaged.

In all the cases of celiac disease, as well as in a number of the control cases, glucose tolerance tests were also made. Although "flat" glucose tolerance tests were obtained in the celiac group as compared with the nonceliac group, the differences were not so striking as those shown by the vitamin A absorption test. Furthermore, there were a number of tests in the celiac group which showed almost normal glucose tolerance curves. (Tables I, II, V, and Chart 2.)

Stool fat determinations show no difference between the celiac group and the control group if the mean of all determinations is considered (31.4% ± 1.6 and 33.3% ± 1.6, respectively). However, it must be remembered that in the cases of celiac disease most stool specimens were taken while the patients were on low fat diets which would necessarily reduce the percentage of fat in the stools. If only the determinations made on the patient before treatment was begun are considered, the mean value of the percentage of fat in the stools of patients with celiac disease was higher than in the control group, although the small number of cases precludes any statistically valid conclusion.

CASE REPORTS

Brief summaries of the cases of celiac disease are presented here. No attempt is made to present these cases in detail although most of them had quite complete hospital study.

CASE 48.—Male, 14 years old, was admitted February, 1935. Chief complaint was pallor and loss of weight; he had always been small for his age. Loss of appetite had started 5 years previously; for one year abdomen had been becoming larger; for

three months stools had been larger and more frequent than normal; pallor had been noted for three months. Physical examination showed an underdeveloped and undernourished Italian boy with pale skin and a large protuberant abdomen. Otherwise he seemed to be normal. Weight was 30.8 kilograms (68 pounds) and height was 138 centimeters (54 inches). Laboratory findings showed a mild secondary anemia, but no other abnormal findings except those considered characteristic of celiac disease (Table II). These are (1) high fat content of the stools; (2) flat sugar tolerance curve; (3) flat vitamin A absorption curve; (4) low total plant pigments in the blood. On a celiac regime the boy gained weight and at the time that he was last seen in October, 1937, two years and eight months after first admission, he had gained 21 kilograms (46 pounds) in weight and 24 centimeters (9.5 inches) in height. No symptoms at that time.

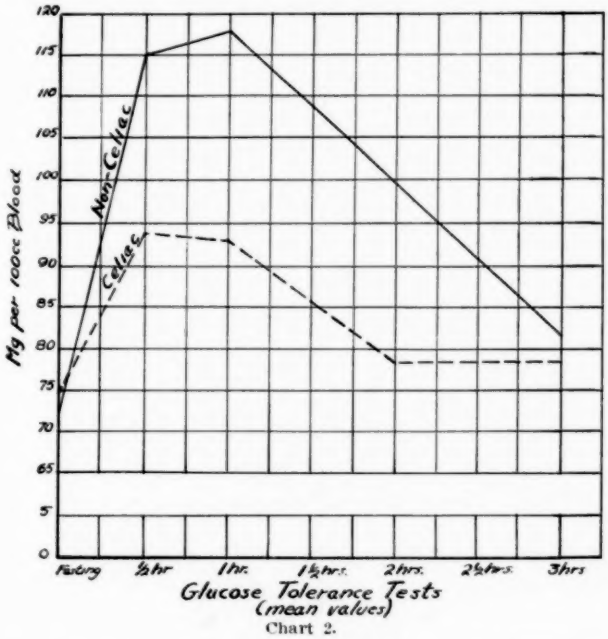

Chart 2.

CASE 49.—Male, 7 years old, was first admitted in November, 1935. Chief complaint was abdominal pain, nausea, and headache associated with an enlarging abdomen and loss of weight. The exact time of onset could not be determined. His appetite was good, and the stools, although yellow and foul smelling, were not unusually large. Physical examination showed a somewhat undernourished Italian boy of 7 years with a large abdomen, old rachitic changes in the chest, and a palpable liver. The remainder of the examination revealed nothing abnormal. Weight was 18 kilograms (38 pounds) and height 115 centimeters (45 inches). Laboratory findings were normal except for a mild secondary anemia and changes considered characteristic of celiac disease. On treatment with a celiac diet and high vitamin intake the boy improved slowly. He was last seen in May, 1938, two years and six months after his first admission. At that time he had gained 4.6 kilograms (10 pounds) and was free of symptoms despite only fair cooperation.

TABLE V

GLUCOSE TOLERANCE CURVES IN PATIENTS ON WHOM VITAMIN A ABSORPTION CURVES WERE MADE

(VALUES EXPRESSED IN MG. PER 100 C.C.)

	NONCELIAC DISEASE				CELIAC DISEASE				
TIME	NUMBER OBSERVATIONS	MEAN AND P. E.	STANDARD DEVIATION AND P. E.	MEDIAN AND P. E.	NUMBER OBSERVATIONS	MEAN AND P. E.	STANDARD DEVIATION AND P. E.	MEDIAN AND P. E.	DIFF. MEANS AND P. E.
Fasting	43	71.8 ± 1.3	12.3 ± 0.9	73.2 ± 1.6	35	74.4 ± 1.6	14.5 ± 1.2	70.6 ± 2.0	−2.6 ± 2.1
½ hour	36	115.0 ± 3.1	26.8 ± 2.2	117.5 ± 3.9	32	93.8 ± 2.4	20.2 ± 1.7	93.0 ± 3.0	−21.2 ± 3.9
1 hour	40	118.2 ± 3.9	37.0 ± 3.8	108.7 ± 3.9	34	93.2 ± 2.3	19.8 ± 1.7	96.0 ± 2.7	−25.0 ± 4.5
2 hours	34	99.7 ± 4.1	35.2 ± 1.9	91.2 ± 5.1	29	78.5 ± 1.8	14.8 ± 1.3	77.5 ± 2.3	−21.2 ± 4.5
3 hours	32	81.2 ± 3.0	25.2 ± 2.1	73.7 ± 3.7	13	78.5 ± 3.1	11.4 ± 2.2	76.6 ± 3.9	−2.7 ± 4.3

CASE 50.—Female, aged 48 years. (Reported in detail by Dr. Samuel Bassett.[9]) Her first admission was in December, 1932, after several admissions to other hospitals. Her story of illness was long and confused. Apparently she had had tuberculous peritonitis in childhood. In her twenties she had had bouts of diarrhea with large, pasty, somewhat frothy stools. She was known to have had pyelitis about eight years before her first admission, but her chief complaints when she came to the hospital were pain in the back, loss of 20 pounds of weight, urgency and frequency of urination, swelling of the legs, and bouts of diarrhea with white, large, frothy stools, and a sore tongue. She had also had cramps in the hands and feet. Physical examination showed an undernourished and chronically ill woman with a large abdomen. Blood pressure was 90/50. There were marked muscular atrophy and some pigmentation of the face, neck, and mouth. Adhesions giving rise to partial intestinal obstruction were released by operation. She was also given liver therapy. There was some improvement, but the symptoms were not relieved entirely, and she was again admitted in February, 1936, because of a pathologic fracture of the head of the femur as a result of marked osteoporosis. On this admission she showed the characteristic laboratory findings of celiac disease and in addition a low calcium content of the blood, which led to typical tetany during her stay. Blood phosphorus was also low. With treatment for steatorrhea she improved somewhat. She was last seen in October, 1936, when she had gained 6 kilograms (13 pounds) over her weight in February.

CASE 51.—Male, 18 months old, was admitted in May, 1935, because of failure to gain weight for the preceding three months, large, gray, but not foul-smelling, stools, and a large abdomen. Physical examination showed an undernourished child with a large abdomen and wasting in the gluteal region. Weight was 8.7 kilograms (19 pounds). Laboratory findings were characteristic of celiac disease. The child was last seen at 4 years of age with an acute pharyngitis. Except for a mild secondary anemia, the youngster had apparently developed normally on a celiac regime.

CASE 52.—Male, 4 years old, was admitted in February, 1936. The onset of symptoms occurred about 2½ years previously with anorexia, loss of strength, pallor, and abdominal swelling associated with periodic bouts of diarrhea in which large, pale, frothy, foul-smelling stools were passed. Physical examination showed a poorly developed and nourished boy of 4 years with a large abdomen and moderate wasting in the gluteal region. Weight was 15.2 kilograms (33 pounds); height 102.5 centimeters (41 inches). The laboratory findings revealed a moderate secondary anemia and the findings characteristic of celiac disease. The patient was put on a celiac diet and observed in the metabolic clinic. The cooperation was poor. The anemia was persistent. Patient was last seen in February, 1937, one year after admission. At this time he weighed 19.7 kilograms (43.5 pounds), a gain of 4.5 kilograms (10.5 pounds). Condition was fair at this time.

CASE 53.—(Reported in detail by Dr. Samuel Bassett.[9]) Male, 43 years old, was first admitted in December, 1936. He had had attacks of diarrhea all his life, especially under nervous tension. For four months previous to admission a prolonged bout of diarrhea had occurred, associated with weakness, anorexia, and weight loss. There had also been abdominal distention and symptoms suggestive of carpal spasm. Physical examination showed a thin, pale man with a protuberant abdomen. Weight was 53.3 kilograms (117 pounds). Laboratory findings were typical of celiac disease. There were a marked lowering of blood calcium and phosphorus (calcium 6.7 mg. per cent and phosphorus 1.36 mg. per cent) and a mild secondary anemia. Patient was put to rest and advised to follow a celiac regime. He was last seen in June, 1938, in excellent condition. Weight at this time was 63.3 kilograms (140 pounds), a gain of 10 kilograms (22 pounds) in a year and a half.

CASE 54.—Female, aged 4 years, was first admitted in May, 1931. Since the child was 11 months old, she had refused to eat, was irritable, and had failed to gain weight well. At 2 years of age she was said to have weighed 11 pounds, which was two pounds less than she weighed at 11 months. The abdomen had become prominent, and four weeks before admission she had persistent diarrhea. Stools were large, pasty and foul smelling. Physical examination showed an undernourished, chronically ill child of 4 years weighing 9.7 kilograms (21 pounds). Laboratory examination showed a moderate anemia and a high percentage of fat in the stools, but vitamin A absorption tests and glucose tolerance tests were not done at this time. The child was taken home against advice. Her course since that time had been one of numerous hospital admissions, usually with improvement while she was in the hospital and recurrence of trouble when she went home. Vitamin A absorption and sugar tolerance curves have been persistently low. She has always been below normal in height and weight. Cooperation at home on the celiac regime has been poor. She was last seen in October, 1938, seven years and five months after first admission. At this time she weighed 22.4 kilograms (49 pounds) and was 123 centimeters (49 inches) tall. She was taking lextron orally and seemed to be improving.

CASE 55.—Female, aged 5 years, was first admitted in September of 1937. For three months before admission the child had been having large bulky diarrheal stools. For one month abdomen had been enlarging. There had been no weight gain for one year. Physical examination showed a fairly well developed and nourished child of 5 years, rather small for her age. Weight was 16.5 kilograms (36 pounds) and height 100.5 centimeters (40 inches). Laboratory examinations showed the typical findings of celiac disease. On a celiac regime the child did quite well. She was last seen in June, 1938, at which time she weighed 18.2 kilograms (40 pounds); there were no further bouts of diarrhea.

CASE 56.—Female, aged 11 years. She was first admitted to the hospital in November, 1932. She had always been small and came to the hospital because of failure to gain, anorexia, fatigue, and bouts of diarrhea which she had had periodically "for a long time." Physical examination showed a poorly developed and poorly nourished 11-year-old Italian girl with a large abdomen. Weight was 19.6 kilograms (43 pounds), and height was 113 centimeters (45 inches). The laboratory examinations showed a moderate anemia, secondary in type, and the typical findings of celiac disease. She was put on a celiac diet on which she gained fairly well, although breaks in the diet were frequent. Her last visit was made to the out-patient department in November, 1938. At this time she weighed 37 kilograms (77 pounds) although she was 17 years old, but she had no complaints.

CASE 57.—Male, aged 11 years. He was first admitted in November, 1934. He had had diarrheal stools, anorexia, and fleeting joint pains and dizziness since December, 1933. He had been followed in the cardiac clinic in the out-patient department for eight months before admission. About three months before admission he had been short of breath and had edema of the ankles. Extrasystoles had been present for at least eight months prior to admission. Physical examination showed a fairly well-developed, but small, pale boy of 11 years. Weight was 26.6 kilograms (58 pounds). There was questionable enlargement of the heart and a soft apical systolic murmur, but otherwise the results of the examination were normal. Laboratory examination showed a rather marked secondary anemia, a vitamin A absorption curve which was flat on three occasions, plant pigments which were below normal, one normal and one "flat" glucose tolerance test, and a moderately increased amount of fat in the stools. Electrocardiogram was normal except for the presence of extrasystoles. Although the diagnosis of celiac disease was not as clear as it was in some of the other cases, it was felt that the boy had enough of the characteristics of the disease

to warrant a trial on the celiac regime. On this treatment he gained well, and cardiac and joint symptoms cleared up. He was last seen in August, 1938, when he was in good condition and weighed 46.2 kilograms (102 pounds).

CASE 66.—Male, aged 15 months, was admitted in October, 1938. At two weeks of age the patient began having bouts of diarrhea with stools which were butterlike in consistency. He was partially breast fed until one month of age when he was completely weaned from the breast. Stools had continued to be frequent, varying in number from two to twelve daily, sometimes associated with blood and mucus. His weight had varied between 14 and 18 pounds for the three or four months preceding admission. Numerous changes in formula were of little help. Transfusions of whole blood and parenteral injections of fluid had been necessary. He had been studied in several clinics in other cities. Appetite had always been fairly good. Physical examination showed a markedly undernourished child weighing 6.8 kilograms (15 pounds). Laboratory examination revealed a normal sugar tolerance test (glucose), high fat content in the stools, all of which were split fats, somewhat low plant pigments in the blood, and an extremely low vitamin A absorption test. It was felt that this child might represent a case of cystic fibrosis of the pancreas. He was placed on a celiac diet with pancreatin, and in the five days which he was in the hospital he gained 500 grams. He had not returned for a check up at the time this paper was written.

COMMENT

In this series of cases of celiac disease vitamin A was not absorbed normally. In all 10 cases before treatment, the vitamin A content of the blood was low. After treatment, the fasting level rose, but the ability to absorb vitamin A was still markedly under that of the controls. This observation was first made by Chesney and McCoord.[1] This suggests that the treatment with a high protein, low fat, low carbohydrate diet modifies, but does not alter, one of the underlying characteristics of the disease—the inability to absorb vitamin A in a normal manner. Although in none of our cases did the ability to absorb vitamin A return to normal under treatment, those patients who did best on this treatment were not retested in the period in which they seemed clinically well. Dr. Charles May, who has used a similar technique for testing vitamin A absorption in cases of celiac disease at the Boston Children's Hospital, informs us that some of his patients who recovered did also regain normal ability to absorb vitamin A.

In our single case of suspected pancreatic fibrosis, the patient was practically unable to absorb vitamin A. In two cases of this condition reported in Blackfan and May's article[7] on the pancreatic lesions associated with fibrosis, vitamin A absorption was extremely slow, but it did occur if sufficient vitamin A was given over a prolonged period. In five of their seven patients showing histologic evidence of vitamin A deficiency, no accessory vitamin A had been supplied in the diet. This may account for the evidence of deficiency of vitamin A in 10 of the 44 cases of cystic fibrosis of the pancreas reported by Anderson.[5] However, depancreatized dogs are unable to absorb vitamin A well,[6] and it is only reasonable to suppose that inability to absorb the vitamin normally was largely responsible for the vitamin A deficiency.

There is this same inability to absorb vitamin A in celiac disease, but apparently it is less marked than in cystic fibrosis of the pancreas. Probably there is sufficient absorption over a prolonged period to prevent the occurrence of clinical or pathologic evidence of vitamin A deficiency, which would account for the lack of evidence of vitamin A deficiency in most reported cases of celiac disease.

However, the inability seems constant enough to make tests for vitamin A absorption of value in the diagnosis of celiac disease. As has been shown, other disease entities may also be associated with inability to absorb vitamin A, so that the flat curve obtained in celiac disease is not pathognomonic.

In a number of cases of diseases of the liver the vitamin A absorption has been abnormal. These cases will be reported later in another paper.

SUMMARY

Patients with celiac disease are unable to absorb vitamin A normally and when given a large amount of vitamin A by mouth do not show an increase in the blood vitamin A equal to that of a group of children with other diseases.

This inability of the patient with celiac disease to absorb vitamin A is usually associated with a flat sugar tolerance curve, increased per cent of fat in stools, and low carotenoid pigments in the blood.

This inability to absorb vitamin A normally, although characteristic of celiac disease, does occur in other diseases and is, therefore, not pathognomonic of celiac disease.

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A TEST FOR THE DETERMINATION OF THE VITAMIN C STORAGE

VITAMIN C INDEX

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VITAMIN C is so widely distributed in nature and so readily stored in the body that it is, at first glance, surprising that deficiencies of it should be at all frequent. That they do develop is due to several factors: (1) destruction of the vitamin before the food containing it is ingested; (2) circumstances which militate against the ingestion of sufficient vitamin; and (3) conditions in which the requirement of the vitamin is increased above the normal.

The chief factors that cause destruction of the vitamin are heating in the presence of oxygen, alkalinity, contact with certain metals, and exposure to light. As a result of any of these, the actual intake may be far less than would be expected from the composition of the diet.

Among the circumstances which militate against the ingestion of an adequate intake in civilized parts of the world may be mentioned alcoholism, which results in loss of appetite for foods containing this factor. Patients on special diets, as for example those for gastric ulcer, and inmates of psychopathic hospitals who present feeding difficulties are also likely to have their intake of this vitamin neglected. By far the largest group consists of infants and young children who, because of either parental ignorance or difficulties encountered in training, are allowed to go without supplements containing this essential factor.

Partial deficiency of vitamin C is not uncommonly associated with illness of any kind. The plasma vitamin C in hospital inmates is, on the average, below the normal figures. Although failure of appetite, poor absorption, and sometimes low gastric acidity contribute toward this result, much evidence has now accumulated which indicates that in febrile conditions with increased metabolic rate the demand for this vitamin is actually greater and the supply, therefore, more readily exhausted. Whether there exist individuals, apparently healthy, who absorb vitamin C with difficulty and require more than the normal quantity taken by mouth to supply their needs has not, as yet, been established. Some clinical evidence suggests that this is the case, but unfortunately a history of adequate intake prior to the development of scurvy cannot always be trusted.

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The fact that scurvy can at times have serious consequences, the probability that even in mild deficiency states resistance to infection is lowered, and the ease with which deficiency of vitamin C can be overcome—all these have made the early recognition of such deficiency a matter of paramount importance.

Many procedures have been employed in attempting to measure vitamin C deficiency in its early stages. The *x-ray changes* leave much to be desired in the way of sensitiveness even in infants; they scarcely ever occur in the case of older children and adults. The *capillary fragility test*, according to most investigators, is not sufficiently reliable[1]; neither is the *fading test with intradermally injected dye* (2, 6 dichlorophenolindophenol).[2] With either one of these latter procedures statistical differences can be demonstrated between individuals on adequate and inadequate intakes of vitamin C, but the extent of the scattering of the figures destroys the usefulness of the tests in individual cases. Also, the tests are not specific for vitamin C, inasmuch as the results are influenced by other factors in addition to the vitamin C nutrition.

The development of chemical methods for the estimation of the vitamin in the blood, the tissues, and the excreta has made possible a great advance in the study of deficiency before the development of clinical scurvy. It is now known that considerable amounts of vitamin C may be stored in the tissues. When the intake is low, the stores become depleted, nearly all the vitamin available is used for metabolic purposes, and very little escapes in the excreta. Under these circumstances when vitamin is administered it goes first to replenish the stores; only when the stores have been sufficiently replenished does the vitamin appear in appreciable amounts in the urine.

The *daily excretion of vitamin C in the urine* was first employed to measure deficiency, since there is a rough parallelism between the output by this route and the intake of the vitamin. This test did not, however, prove satisfactory. Marked individual variations were encountered. In reviewing the situation, Ingalls[3] makes the comment: "It is apparent that so many factors, including renal function, affect the excretion of the vitamin, that the reducing power of the urine cannot be considered as a simple and reliable index of ascorbic acid nutrition."

Saturation tests were then introduced by Zilva and by Abbasy, Harris, and Ray, the vitamin output in the urine being studied after the administration of vitamin C by mouth. An individual whose stores are deficient will excrete a relatively small proportion of the intake in twenty-four hours; one with adequate stores a definitely greater portion. If large doses are administered over a period of days, the per cent of the intake excreted in the urine increases, reaching 50 per cent or more in three to fifteen days, after which a "state of saturation" appears to be reached and the output remains constant as long as the same intake is maintained. The time required for this state of saturation to be reached is a measure

of the stores at the onset of the experiment—the sooner saturation is reached the better were the stores. The reliability of this test has not been questioned, but it possesses several practical disadvantages. It requires several days and numerous titrations of urinary samples. The collection of twenty-four-hour specimens in infants requires placing them on a frame, a procedure which is a hardship for subjects who are likely to have tender extremities.

Urinary tolerance tests were used by Portnoy and Wilkinson,[2] Ralli and co-workers,[5] Wright and co-workers,[6] and others. The procedures in brief are as follows: After a parenteral injection of a massive dose of vitamin C, the urinary excretion is followed for either three or five hours. It is unnecessary to follow the excretion for longer periods in adults because after a massive dose about 80 per cent of the total twenty-four-hour vitamin C excretion occurs within this period. Those on a deficient diet excrete much less than individuals on a normal diet. The method is suitable for adults, but for infants and small children it is again objectionable, because a frame is required and because of difficulty in obtaining voided specimens at the proper time, especially in the oliguric scorbutic children.

A further advance was made with the development of methods for the determination of vitamin C in the blood and plasma. Here there are fewer reducing substances which interfere than in urine. The *plasma level of vitamin C* gives considerable information in regard to deficiency. On an adequate intake the fasting values are about 0.7 to 0.9 mg. per cent; only exceptionally are they below 0.5 mg. per cent. Symptoms of scurvy make their appearance only when the plasma value falls to 0.15 mg. per cent or below; often they are well below this. When the plasma level lies between 0.5 and 0.16 mg. per cent, one may be sure that the stores are not optimal, but it is impossible to tell the extent to which they are depleted. The difficulty lies in the fact that the plasma level falls very promptly after the diet becomes deficient. In an experiment on himself van Eekelen[7] found that the fall in the plasma preceded the change in urinary excretion; in twenty days after the beginning of a deficient diet the plasma concentration fell from 1.4 to 0.5 mg. per cent and in two months it had fallen to 0.19 mg. per cent. This rapid fluctuation in the plasma level in response to diet was also noted by Portnoy,[2] who found subnormal plasma values when no gross deficiencies could be found by other tests, and by Wright,[6] who found that three patients, after a week or less on a limited diet had low plasma vitamin C values, although the urinary tolerance test demonstrated that marked tissue unsaturation had not yet taken place. Greenberg[8] maintained that the plasma vitamin C level is a measure of the *immediate* nutritive level, and that a more accurate estimate of the *stores* can be obtained by following daily the plasma vitamin C level while a known vitamin C supplement is given.

Finally, in the last three years, the changes in the plasma vitamin C following a massive dose of the vitamin, administered orally or parenterally, were used as a measure of vitamin C nutrition.

After *oral* administration both Greenberg[8] and Portnoy[2] found a significant rise in the plasma vitamin C in one hour, followed by a gradual fall to approximately the original level. Portnoy found this return to the original level to occur within five or six hours in those on an adequate diet and even earlier (in four hours) in those on a deficient diet. Lund and Lieck[10] determined the plasma vitamin C content before ingestion of the massive dose, and two hours later, and found that at two hours it was above 1 mg. per cent in sixteen normal adults, but not above 0.24 mg. in four scorbutic adults; after satisfactory treatment these latter reacted similarly to the normal group.

To eliminate the factor of absorption, Elmby and With[9] injected 500 mg. ascorbic acid intravenously into a patient with a history of deficient vitamin C nutrition. The plasma ascorbic acid content was determined before injection and eight times within the next four hours. The ascorbic acid content fell rapidly in the first hour, was significantly above the original level after two hours, but returned to the original value in four hours. Portnoy examined the plasma before the intravenous injection of the massive dose and six times in the following five hours. The results of six experiments were shown in a table; in four of these the plasma vitamin C content reached a constant level in four hours, and in the other two, in five hours. The results of a large number of similar experiments, shown only in a composite curve, indicated that this constant level was reached between three and four hours. Wright's investigation similarly showed that three hours after intravenous injection of the vitamin the plasma ascorbic acid content approximated the original level. Both authors found that eighteen to twenty minutes after injection, individuals on a diet adequate in vitamin C had a plasma ascorbic acid content between 6.6 and 11.4 mg. per cent and those on an inadequate diet between 2 and 6 mg. per cent. The plasma vitamin C content at this time was fairly well correlated with the amount of vitamin excreted in the urine during the test.

PRESENT STUDY

The present study was undertaken to investigate the applicability of the parenteral tolerance test to the determination of vitamin C nutrition in infants.*

We have employed the intramuscular rather than the intravenous administration of the vitamin because of its easier technique. The procedure as applied to infants is as follows: After fasting (or a vitamin C

*Working with infants the number of venepunctures had to be reduced to a minimum. Preliminary experiments on infants and normal adults showed that the individual differences in the rate and extent of the absorption of the vitamin from the intestinal canal made the interpretation of *oral* tests difficult, if only two or three venepunctures were performed.

free breakfast) blood is drawn with a *dry* syringe to avoid hemolysis. Lithium oxalate (1 c.c. of 0.7 per cent solution evaporated to dryness in a bottle calculated to receive 5 to 8 c.c. blood) is used as anticoagulant. One drop of a 5 per cent potassium cyanide solution* is used to prevent enzyme action. The plasma is then separated immediately, and the vitamin C content determined as described by Ingalls.[3] Immediately after the first sample of blood has been taken, the intramuscular injection of 200 mg. cevitamic acid, dissolved in 5 to 8 c.c. saline, is given. Four hours later a second sample of blood is taken and analyzed.

TABLE I

DATA ILLUSTRATING THE SUITABILITY OF THE FOUR-HOUR OBSERVATION PERIOD (PLASMA VITAMIN C CONCENTRATION)

CASE NO.	BEFORE	AFTER INJECTION					
		10 MIN.	18 MIN.	45 MIN.	2 HR.	4 HR.	24 HR.
1	Traces	–	–	–	–	0.14	0.12
2							
First test	0.05	–	–	–	–	0.06	0.06
Second test	0.06	–	–	–	–	0.21	0.24
3	Traces	–	–	–	–	0.13	0.13
12	0.01	–	–	–	0.08	0.08	–
14							
First test	Traces	–	–	–	–	0.16	0.10
Second test	0.10	–	–	–	–	0.34	0.28
17							
First test	0.05	–	–	–	0.49	0.09	–
Second test	0.44	–	–	–	1.95	1.33	–
18							
First test	0.04	–	3.22	–	–	0.07	0.08
Second test	0.08	–	–	1.56	–	0.25	0.22
29	0.14	4.4	–	–	–	0.47	–

NOTE.—The bulk of the injected vitamin is absorbed within ten minutes (Case 29), and diffuses from the plasma very rapidly (Case 18). Two hours after injection the plasma may or may not have reached the constant level. Contrast Case 12 with 17. Cases 1, 2, 3, and 18 indicate that at four hours the plasma level had become constant since essentially the same values were obtained twenty-four hours later.

The use of the four-hour interval is based on observations of Greenberg,[8] Elmby,[9] Portnoy,[2] their co-workers, and ourselves on adults as to the behavior of the plasma vitamin C after a parenteral injection. The plasma value rises promptly after such an injection, then falls rapidly, and usually by the end of four hours has reached a level which remains relatively constant during the next twenty-four hours. As we have mentioned before, after a massive parenteral dose of vitamin C, 80 per cent of the total twenty-four-hour excretion takes place within the first four or five hours. Therefore, the amounts excreted during the remainder of the twenty-four-hour period and utilized in the metabolic processes are not great enough to alter this constant plasma value. This constant level was obtained in those patients with scurvy or deficient stores who

*The use of cyanide has been criticized on the ground that it itself would reduce the dye. Studies we have made with the Kahlbaum preparation which we used have failed to confirm this. Our cyanide solution alone did not reduce the dye, nor did its addition alter the titration value of a known vitamin C solution at concentrations comparable to blood at pH 2 and at pH 4.5.

The 5 per cent metaphosphoric acid was freshly prepared every three days and kept in the ice box. The dye was standardized against a known solution of vitamin C.

TABLE II

GENERAL TABLE VITAMIN C TEST*

CASE NO.	RACE	AGE	DIAGNOSIS	DIET	SAMPLE (IN MG. %) I	II	INCREASE (MG. %)	INDEX	REMARKS
				Group 1					
1	W	7 mo.	Scurvy.	Never on breast. No green vegetables. O.J. very irregularly.	Traces	0.14	0.14	0.14	For 9 days cried if legs were touched. Scorbutic rosary. Tourniquet test negative. Few R.B.C. in urine. X-ray: positive.
2	W	10 mo.	Scurvy.	On breast 4 mo. No green vegetables. O.J. ½ oz. since 2 mo. old, but "spits out most of it."	0.05	0.06	0.01	0.05	Tender limbs for 2 wk. Scorbutic rosary. X-ray: positive.
3	C	8 mo.	Scurvy. Pachymeningitis.	On breast 2 mo. Received about 8 oranges all her life. No green vegetables. Vomited often since 4 mo. old.	Traces	0.13	0.13	0.13	"Cold" for 2 days. Brought in for failure to gain. Vomiting worse for several days. Fontanel tense. Subdural puncture revealed bloody fluid. X-ray: positive.
4	W	12 mo.	Scurvy.	On breast 2 mo. O.J. given for 1 week, when 4 mo. old; vomited, so abandoned. Refused green vegetables.	0.06	0.08	0.02	0.12	For 2 wk. refused to stand, cried if touched; bleeding gums. Scorbutic rosary. Cutaneous hemorrhages. Few R.B.C. in urine. X-ray: positive.
5	C	17 mo.	Scurvy.	On breast 1 mo. O.J. 1-2 oz. between 4-8 mo. Discontinued because it caused "loose bowels." No green vegetables.	0.03	0.25	0.22	0.66	Hemorrhagic gums. Tender legs. X-ray: positive.

*Sample I = plasma vitamin C level before injection of 200 mg. intramuscularly.
Sample II = plasma vitamin C level 4 hrs. after injection of 200 mg. intramuscularly.
Increase = Sample I—Sample II.
Index = Sample I × Increase × 100.

TABLE II—CONT'D

6	W	7½ mo.	Scurvy.	Never on breast. Mother insisted that patient received O.J. 1½ oz. daily, and did not vomit it.	0.03	0.11	0.08	0.24	For 5 days did not move her legs, cried when touched. Scorbutic rosary. (Urine not examined—disp. patient.) X-ray: positive.
7	W	10 mo.	Scurvy. Acute nutritional disturbance.	Nursed 3 wk. O.J. and green vegetables tried, but refused, abandoned. Diarrhea for 3 wk.	0.09	0.17	0.08	0.72	Hb. 45%. Extremities were not tender, nor was rosary found. Gums were normal. X-ray: positive.
8	W	10 mo.	Scurvy.	Nursed 1 day. O.J. 1 oz. from 2 to 4 mo. Discontinued for economic reasons.	0.08	0.14	0.06	0.48	Tender limbs for 3 wk., swollen legs & feet for 2 wk. "Black eyes" 2 wk. ago; bleeding gums. Scorbutic rosary. R.B.C. in urine. X-ray: positive.
9	W	12 mo.	Scurvy.	On breast 1 mo. No green vegetables. Twice was given ½ orange.	Traces	0.10	0.10	0.10	Tender limbs. Benzidine test positive in urine. Petechiae on trunk and arms. Gum changes. Scorbutic rosary. X-ray: positive. In the test 400 mg. ascorbic acid were injected.
10	W	9 mo.	Scurvy.	Never nursed. O.J. 2 days at age of 1 mo., and last 2 days before admission, 1 oz.	0.04	0.20	0.16	0.64	Right leg tender for several weeks, thighs swollen—diagnosed by neighbor. Boggy, hemorrhagic gums. Scorbutic rosary. R.B.C. in urine. X-ray: positive.
11	C	9 mo.	Scurvy. Malnutrition.	Never on breast. O.J. 1 tsp. at 1 mo.; later 2 tsp. She "spits it out the last 7 mo." For 2 wk. refuses most of the food.	0.08	0.11	0.03	0.24	Tender extremities. Scorbutic rosary. Rapid pulse. X-ray: positive.
12	W	10 mo.	Scurvy.	Never on breast. O.J. offered, but baby always vomited it; abandoned.	0.01	0.08	0.07	0.07	For over a month cried when legs were moved. No gum changes, although had 3 teeth. Scorbutic rosary. Rapid pulse. X-ray: positive. Plasma vitamin C 2 hr. after injection 0.08 mg. %.

TABLE II—CONT'D

CASE NO.	RACE	AGE	DIAGNOSIS	DIET	SAMPLE (IN MG. %) I	II	INCREASE (MG. %)	INDEX	REMARKS
13	C	8 mo.	Scurvy. Pachymeningitis.	Never on breast. O.J. never given. Never took feedings well. Recently vomiting.	0.10	0.14	0.04	0.40	Gums normal. Scorbutic rosary. Extremities not tender. Quite irritable. X-ray: positive.
14	W	8½ mo.	Scurvy.	Never on breast. O.J. never given. No green vegetables.	Traces	0.16	0.16	0.16	Cross on handling for several weeks. Gums purplish. Rosary more suggestive of rickets. Thighs swollen. Legs tender. R.B.C. in urine. X-ray: positive.
15	C	10 mo.	Scurvy. Malnutrition.	Never nursed. No O.J. or green vegetables.	Traces	0.15	0.15	0.15	Tender limbs. Petechiae on feet. Scorbutic rosary. X-ray: positive.
16	W	9 mo.	Scurvy.	On breast 1 wk. O.J. 1½ oz. allegedly given daily. Recently green vegetables.	0.13	0.17	0.04	0.52	Restless for 1 week. Scorbutic rosary. Cardiac failure. Extremities not tender. X-ray: positive.
17	W	13 mo.	Scurvy.	Never on breast. O.J. 1 oz. since 2 mo. old.	0.05	0.09	0.04	0.20	Tender extremities for 2 wk. Frequent upper respiratory infections. Poor appetite. Scorbutic rosary. (Urine not examined—disp. patient.) X-ray: positive.
18	W	10 mo.	Scurvy.	Nursed a few days. Vegetables, O.J. refused, abandoned.	0.04	0.07	0.03	0.12	For 1 mo. cried if picked up. Swollen, bluish hemorrhagic gums a few days before admission. Tourniquet test strongly positive. Scorbutic rosary. Urine negative. X-ray: positive.
19	W	17 mo.	Scurvy. Birth injury.	Breast fed 2½ mo. O.J. 2 tsp. from 1 to 4 mo. Green vegetables irregularly.	0.03	0.15	0.12	0.36	Convulsions. Scorbutic rosary. No gum changes. Legs not tender. Rapid heart rate. X-ray: negative.

TABLE II—CONT'D

20	W	5½ mo.	Rickets. Scurvy. Eczema.	Never on breast. O.J. 2 tsp. from 4 to 13 wk., abandoned because of eczema.	0.01	0.13	0.12	0.17	Fever for 5 days. Scorbutic rosary. Gums normal. Extremities questionably tender. X-ray: rickets only.
21	C	6 mo.	Scurvy.	Never nursed. O.J. 1 oz., allegedly given except for the last 3 wk.	0.04	0.06	0.02	0.08	Frequent colds. Failure to gain. Extremities tender for 2 wk. No gum changes. Scorbutic rosary. No x-ray. (Mother neglected to go to X-ray Department.)
22	C	6 mo.	Scurvy. Pneumonia.	On breast 1 mo. O.J. now and then since 4 mo. old.	Traces	0.09	0.09	0.09	Brought in for otitis media. On P.E. pneumonia and tender limbs found in addition. X-ray: rickets only.
				Group 3†					
23	C	14 mo.	Congenital glaucoma.	Never nursed. O. J. given irregularly, maybe 1 glass a wk. Green vegetables now and then.	0.15	0.32	0.17	2.5	Brought in for her eye condition. No evidence of scurvy.
24	C	5½ yr.	Malnutrition	Eats 1 orange daily (?) except the last month. No green vegetables.	0.02	0.60	0.58	1.2	Neglected child. Gums normal. Urine negative. X-ray shows retardation of bone-age.
25	W	18 mo.	Rickets. Malnutrition.	O. J. ½ oz. given daily.	0.08	0.44	0.36	2.9	Cold and diarrhea for 1 wk. X-ray: negative.
26	C	22 mo.	Rickets.	Never on breast. Received O. J. since 1 yr. old every day (?). Green vegetables only occasionally.	0.07	0.23	0.16	1.1	Brought in for weak bones. X-ray: marked rickets with deformities. No evidence of scurvy.
27	C	8 mo.	Eczema. Tetany.	Nursed for 1 wk. O. J. was never given. No green vegetables.	0.04	0.38	0.34	1.3	Undernourished. Tetany (Convulsions, Ca 5.1 mg. %). X-ray: healing rickets. No sign of scurvy.

†Group 2 consists of patients from Group 1 after 1 parenteral treatment.

TABLE II—CONT'D

CASE NO.	RACE	AGE	DIAGNOSIS	DIET	SAMPLE (IN MG. %) I	II	INCREASE (MG. %)	INDEX	REMARKS
28	W	10 mo.	Medulloblastoma	Breast for 2 mo. Vegetables daily. O. J. 1 oz. since 4 mo. old, recently 2 oz. Vomited everything last 9 days.	0.12	0.47	0.35	4.2	Projectile vomiting. Bulging fontanel. Lumbar puncture: xanthochromic fluid. Test done because of possibility of pachymeningitis.
29	C	22 mo.	Malnutrition. Wt. only 4700 gm.	Diet was always poor. Milk only once or twice a week. Green vegetables occasionally. 1 orange daily between 6th and 21st mo.	0.14	0.47	0.33	4.6	Frequent diarrhea alternating with constipation. Dehydration. Marasmus. Hb. 30%. No sign of scurvy. X-ray: negative. 10 min. after injection plasma vitamin C: 4.4 mg. %.
				Group 4‡					
30	C	11¼ mo.	Scurvy. Pneumonia. Otitis media.	Breast fed, supplemented with cow's milk. Cereals and green vegetables; while O. J. was given very rarely.	0.21	0.70	0.49	10.3	Patient favored left wrist, which was swollen. Joint puncture, blood culture negative. Pneumonia. X-ray: scurvy. Mastoidectomy done. Test performed 12 wk. after admission.
31	W	9 mo.	Scurvy.	Never on breast. Had altogether only 2 oranges before admission, because it caused diarrhea.	0.17	0.92	0.75	12.6	Diarrhea on and off. Limbs were tender for several wks. X-ray: scurvy. Treated as dispensary patient. Test done 3 wk. after the treatment.
32	W	13 mo.	Pneumonia. Scurvy.	Fed on unboiled cow's milk. Vegetables once a week, no O. J.	0.08	0.37	0.29	2.3	Pneumonia with encapsulated fluid. Screamed if handled. Scorbutic rosary. X-ray: scurvy. Urine negative. Test 20 days after treatment.

‡This group consists of patients from Group 1 after 2 or more parenteral treatments, with the addition of these 4 cases, who were too critically ill on admission to be studied before treatment.

TABLE II—CONT'D

33	W	9 mo.	Scurvy. Heart failure.	Never nursed. No O. J. or green vegetables.	0.24	0.61	0.37	9.0	Cough for 2 wk.; on day of admission patient seemed peevish, turned blue, vomited. Labored respiration. Cried if touched or handled. Scorbutic rosary. Liver 4 fingerbreadths below costal margin. Heart enlarged. Gallop rhythm. Digitalized and vitamin C injections and O.J. Test 16 days later.
				Group 5					
34	W	3¼ yr.	Hemolytic streptococcus infection. Anaphylactic purpura. Chronic tonsillitis.	Vegetables since 1 yr. old daily; 1 orange weekly.	0.23	0.54	0.31	7.1	Purpuric spots on feet and ankles. Platelets: normal number. Urine negative. Tourniquet test negative.
35	W	2¼ yr.	Celiac disease. Otitis media.	O. J. started at 6 wk. 1 orange daily since 1 yr. old, except the last 2 mo. In hospital received 4 oz. O. J. for 10 days before the test.	0.18	1.79	1.61	29	Large, foamy stools. Distended abdomen. Failure to grow. Apathetic. Patient had edema at time of test, absorption may have been slow.
36	W	20 mo.	Harelip.	Hospital diet.	0.99	1.46	0.47	46	Brought in for operation.
37	C	7 mo.	Rickets.	On breast for 9 days. O. J. 1 oz. since 1 mo. old, some of which he spits up.	0.24	0.70	0.46	11	No evidence of scurvy. X-ray: rickets.
38	W	2 yr.	Hemolytic streptococcus infection. Anaphylactic purpura.	O. J. regularly. Eats fruits, green vegetables daily.	0.06	0.72	0.66	3.9	Cough for 1 wk. Purpuric rash. Tourniquet test negative. Platelets: 86,000. No gum changes. X-ray: negative.

TABLE II—CONT'D

CASE NO.	RACE	AGE	DIAGNOSIS	DIET	SAMPLE (IN MG. %) I	II	INCREASE (MG. %)	INDEX	REMARKS
39	C	5 mo.	Congenital syphilis. Nephritis.	Breast fed.	0.11	0.67	0.56	6.1	Anemia. Died. Autopsy: syphilis, septicemia, hemorrhagic nephritis.
40	C	10 yr.	Repeated intestinal hemorrhages. Lymphosarcoma?	For 6 wk. prior on liquid diet with as much fruit juice as desired.	0.55	1.25	0.70	39	Brought in because of anemia and intestinal hemorrhage. Lower part of ileum resected. Hemorrhagic tendency.
41	W	7 yr.	Thrombocytopenic purpura.	O. J. and green vegetables daily.	1.28	1.73	0.45	57	Bruised easily. Purpuric spots. Abdominal pain. Platelets: 2,600. Later rose to 75,000.
42	W	7 yr.	Rheumatic fever.	For 2 mo. on liquid diet with as much O. J. or fruit juice as desired.	1.86	2.18	0.32	59	Has been followed in the Cardiac Clinic for over 3 yr. Diet was always adequate with regard to vitamins.
43	W	8½ mo.	Rhinopharyngitis.	*Breast fed.* Vegetables once or twice a week since age of 5 mo. No O. J.	1.05	1.52	0.47	49	Mother's diet consisted practically of cereal, coffee and buns; vegetables and meat once or twice a week. No fruit.
44	C	2½ mo.	Cavernous sinus thrombosis? Tetany?	*Breast fed.* O. J. occasionally given.	0.27	1.03	0.76	20	Patient appeared sick only the day of admission. Comatose, dehydrated, spastic, jittery. Very frequent convulsions. Ca 7.2 mg. %. For 5 days before test patient had *no* feeding—continuous intravenous drip given with *no* ascorbic acid.

were tested for this point. In the case of individuals whose stores were better filled, however, the level of the plasma vitamin C content obtained four hours after the injection did not persist, but decreased somewhat during the following hours. This would naturally be expected, since well-filled stores would have less avidity for the vitamin, and hence the constant level would be obtained more slowly. When the vitamin is injected *intravenously, immediately* after the injection the vitamin C content of plasma must be approximately the same in individuals on a good vitamin intake and in those on a deficient diet. However, the depleted stores are more readily filled than the good depots, therefore the plasma values fall more rapidly. The tests of Portnoy,[2] Lund and Lieck,[10] and Wright[6] are based on this different rate of deposition of the vitamin in the depots, while our test takes as its criterion the end phase of this deposition.

Unless otherwise stated, 200 mg. cevitamic acid was used as a test dose in infants because 100 mg. did not bring out the difference between depleted and poorly filled depots; and larger doses did not accentuate this difference and necessitated longer observation periods.

RESULTS

Seventy tests were performed on forty-four children, thirty-seven of whom were under two years of age. The cases are divided into five groups.

Group 1. Twenty-two patients with manifest clinical evidences of scurvy, such as swollen, bluish or bleeding gums, sharp costochondral junctions, swollen or tender extremities. Eighteen of these patients also showed typical x-ray changes.

Group 2. Scurvy patients after a single treatment with an intramuscular injection of 200 mg. cevitamic acid. These patients are from Group 1.

Group 3. Seven patients in whom a deficiency of vitamin C was suspected from the dietary history or the persistence of vomiting. None of these patients had definite symptoms of scurvy or characteristic x-ray changes.

Group 4. Scorbutic patients from the first group, after more than one treatment, with additional four scorbutic infants who were too sick to be studied before treatment.

Group 5. Eleven patients with nothing to suggest scurvy who were hospitalized for various other conditions.*

Cases of Group 5 could not serve as controls, because of the presence of pathologic conditions that might influence vitamin C metabolism. The same objection applies to all cases admitted to the hospital with a few exceptions. In the Out-Patient Department, on the other hand, the

*These patients are included because of their importance in evaluating the vitamin C metabolism in nonscorbutic cases.

uncertainty of information concerning ingestion of vitamin C precludes the use of these children as controls. We have therefore used as control the behavior of the plasma vitamin C content during the treatment of scurvy (Groups 2 and 4) when the vitamin C depots can be roughly estimated. (See Table VI.)

TABLE III

INITIAL PLASMA VITAMIN C CONTENT (MG. %)

	NUMBER OF CASES	MINIMUM	MAXIMUM	AVERAGE	REMARKS
Group 1	22	Traces	0.13	0.04	Untreated clinical scurvy.
Group 2	6	0.06	0.13	0.09	Scurvy after one treatment.
Group 3	7	0.02	0.15	0.09	Cases with suggestive history of vitamin C deficit, but no symptoms of scurvy.
Group 4	23	0.17	0.80	0.38	Scurvy after two or more treatments.*
Group 5	11	0.06	1.86	0.62	Miscellaneous cases.

*Case 32 was disregarded in Group 4. This patient received the *usual* treatment, but was suffering from empyema, and obviously in the presence of such severe infection a much greater amount of vitamin would be necessary to replenish the depots.

TABLE IV

FINAL PLASMA VITAMIN C CONCENTRATION FOUR HOURS AFTER INJECTION

	NUMBER OF CASES	MINIMUM	MAXIMUM	AVERAGE	REMARKS
Group 1	22	0.06	0.25	0.13	Untreated clinical scurvy.
Group 2	6	0.21	0.68	0.44	Scurvy after one treatment.
Group 3	7	0.23	0.60	0.41	Cases with suggestive history of vitamin C deficit, but no symptoms of scurvy.
Group 4	23	0.55	1.54	0.93	Scurvy after more than one treatment.*
Group 5	11	0.54	2.18	1.18	Miscellaneous cases.

*Case 32 is disregarded in Group 4 for reasons explained in footnote to Table I, and Case 35 in the Group 5 because the response was unusually high and it might have been due to the fact that the "constant level" in the plasma was not reached at four hours, because of slow absorption of the intramuscularly injected cevitamic acid in the *edematous patient.*

Our observations have confirmed the value of the parenteral tolerance test. From our data it appears clear that deficient vitamin C nutrition may be revealed (a) by the low initial value of the vitamin C in plasma and (b) much better by the final concentration four hours following the injection of the test dose. Even sharper differentiation was possible when both the initial value and the response to the test dose were taken into consideration. We therefore introduced the term "vitamin C index" representing the product of the initial value and the increase in plasma vitamin C four hours after the injection, multiplied by 100.*

*We were looking for a method to determine the state of storage. The plasma level is determined by the intake, the rate of withdrawal from, or deposition into the stores, the rate of excretion, and the rate of utilization. Since the rate of excretion is probably dependent on the plasma level, it is not an independent factor.

The low plasma level therefore may depend on ingestion of inadequate amounts, low stores, increased destruction, or utilization. If the inadequate ingestion or increased destruction is of short duration, then the storage may not be greatly interfered with, although the plasma level is low. In such a case the increase in the plasma vitamin C following the injection of the test dose may be normal or even greater than normal, hence the combination of the initial plasma level and the increase four hours after injection will give a better idea of the state of the stores than either alone. This is the basis of the index.

PLASMA VITAMIN C CONTENT

As expected, the plasma vitamin C content was very low in the scorbutic patients. The values in the second and third groups were higher, but still within the range generally associated with clinical signs of scurvy. In the fourth group the plasma vitamin C concentration was still below the generally accepted lower limit of normal. In the last group the average was in the "normal" range.* The low values in Group 4 were due to the fact that we intentionally interrupted the treatment for reasons to be explained later and thereby provoked a fall in the plasma vitamin content.

It is suggested by the results that the patients in Group 3 had as little vitamin reserves as those with scurvy after the parenteral administration of 200 mg. cevitamic acid. Although the group averages are in agreement with the absence or presence and severity of the deficiency, the individual values overlap and make it obvious that the usual fasting plasma vitamin C determinations are not satisfactory for the diagnosis of scurvy, since some values obtained in Group 3, or even in Group 5, were just as low as in scurvy.

CONCENTRATION OF PLASMA VITAMIN C FOLLOWING A PARENTERAL TEST DOSE

An inspection of Table IV and the individual values given in Tables II and VI shows that with one exception the final concentration was below 0.20 mg. per cent in the scorbutic cases, and between 0.20 and 0.60 mg. per cent when the depletion of the depots was serious (Groups 2 and 3) with one exception. Values greater than 0.60 were obtained in Groups 4 and 5 with four exceptions. Thus in sixty-four out of seventy tests (91 per cent) correct information was obtained by *this single* determination, i.e., the four-hour test.

VITAMIN C INDEX

The findings are shown graphically in Figs. 1 and 2, in which the initial plasma vitamin C values are plotted as abscissae and the *increase* following the test dose as ordinates. The vitamin C indices are shown by the hyperbolic curve in Fig. 1 and the final vitamin C concentrations four hours after the injection are plotted in Fig. 2.

Table V gives the results in the different groups.

It will be noted from an examination of the two graphs that the index is the more satisfactory criterion. It permits a sharp distinction between

*Even in the fifth group five patients had subnormal values; two of these had severe streptococcus infections, one had congenital syphilis and nephritis so severe that he succumbed, one suffered from celiac disease, and the last patient, who had rickets, probably had an actual intake below the minimal requirement as he "spat up some" of his daily ounce of orange juice. None of these patients had an unusually high vitamin C intake, while the other six in this group had a very high vitamin C intake or had no infection.

the cases of active scurvy and those treated once and permits a sharper separation of the cases receiving single and multiple treatment than does the final plasma vitamin C concentration alone.

In active scurvy the index was invariably below 0.8. In patients receiving one treatment the index was regularly between 0.9 and 6.0,

TABLE V

VITAMIN C INDEX*

	NUMBER OF CASES	MINIMUM	MAXIMUM	AVERAGE	REMARKS
Group 1	22	0.05	0.72	0.27	Untreated clinical scurvy.
Group 2	6	0.9	5.7	3.1	Scurvy after one treatment.
Group 3	7	1.1	4.6	2.5	Cases with suggestive history of vitamin C deficit, but no symptoms of scurvy.
Group 4	23	6.3	59	20	Scurvy after more than one treatment.†
Group 5	11	3.9	59	30.8	Miscellaneous cases.

*Vitamin C index = initial value × the *increase* after injection × 100.
†Case 32 in Group 4 and Case 35 in Group 5 are disregarded for reasons explained in footnotes to previous tables.

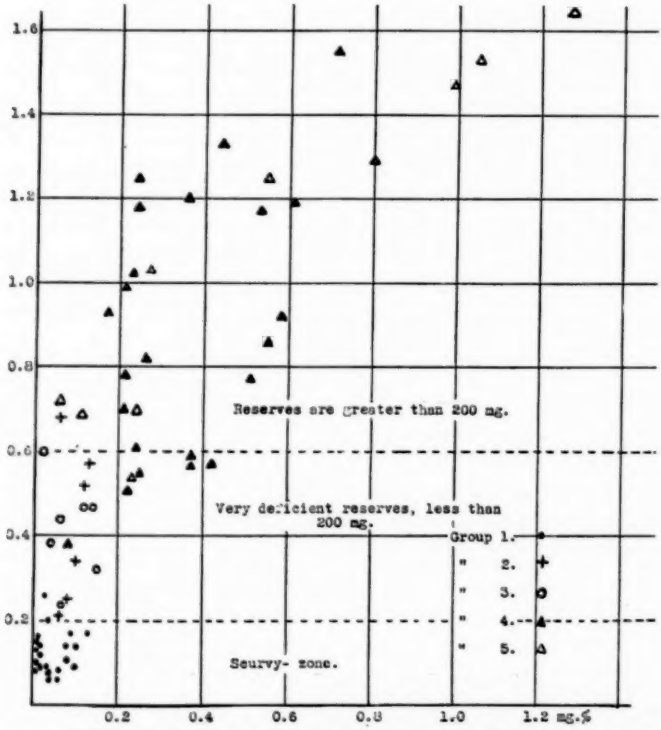

Fig. 1.—Illustrating the final plasma vitamin C concentration four hours after injection. Initial plasma vitamin C is represented by the abscissa; the final concentration is measured by the ordinate. In Figs. 1 and 2 the symbols are the same.

values similar to those obtained in the patients without scurvy on a suspiciously low intake (Group 3). With one exception (Case 32), complicated by pneumonia and empyema, values above 6 were obtained in cases of scurvy after multiple treatments, as was found to be the case also in normal individuals and in most of the hospital inmates in the miscellaneous group. Only one value below 6 was obtained in this last group, in a patient (Case 38) suffering from a severe streptococcus infection.

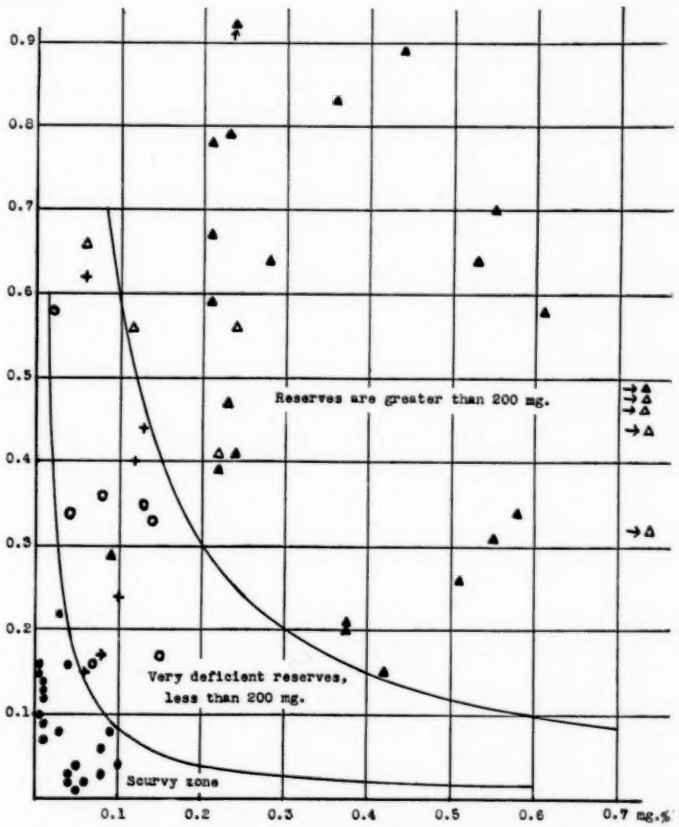

Fig. 2.—Illustrating the vitamin C index. Abscissa measures the initial value, ordinate the "increase" after injection. Symbols are the same as in Fig. 1.

The indices obtained in Groups 2 and 3 indicate that the vitamin C reserves of these two groups are comparable. The indices of Groups 4 and 5 differ from each other. However, if only those patients are considered in Group 4 who received full treatment (i.e., five times 200 mg. vitamin C, at least) the index is 30 instead of 19, pointing to the

TABLE VI

EFFECT OF TREATMENT ON PLASMA VITAMIN C AND ON VITAMIN C INDEX IN SCURVY

CASE NO.	TIME OF TEST	VALUE (IN MG. %) INITIAL	FINAL (4 HR.)	INCREASE (MG. %)	INDEX	PREVIOUS TREATMENT
1.	Before treatment	Traces	0.14	0.14	0.14	None.
	After 1 treatment	0.12	0.52	0.40	4.8	24 hr. before test 200 mg. i.m. Total = 200 mg.
2.	Before treatment	0.05	0.06	0.01	0.05	None.
	After 1 treatment	0.06	0.21	0.15	0.90	24 hr. before test 200 mg. i.m. Total = 200 mg.
	After 2 treatments	0.24	0.55	0.31	7.5	24 hr. before test 200 mg. i.m. Total = 400 mg.
	After 3 treatments	0.58	0.92	0.34	19.7	24 hr. before test 200 mg. i.m. Total = 600 mg.
3.	Before treatment	Traces	0.13	0.13	0.13	None.
	After 1 treatment	0.13	0.57	0.44	5.7	24 hr. before test 200 mg. i.m.
4.	Before treatment	0.06	0.08	0.02	0.12	None.
	After 4 treatments	0.53	1.17	0.64	34	24 hr. before test 200 mg. i.m. Total = 800 mg.
	After full treatment	0.80	1.29	0.49	39	24 hr. before test 4 oz. O. J. Total = 1000 mg. and for 3 days 4 oz. O. J. daily.
5.	Before treatment	0.03	0.25	0.22	0.66	None.
	After 4 treatments	0.21	0.78	0.57	12	24 hr. before test 30 mg. i.m. Total = 1 × 200 and 4 × 30 mg. i.m.
	After full treatment	0.37	0.57	0.20	7.4	24 hr. before test 2 oz. O. J. Total = 520 mg. i.m. and for 6 days 2 oz. O. J. while patient developed pneumonia.
6.	Before treatment	0.03	0.11	0.08	0.24	None.
	After full treatment	0.36	1.20	0.84	30	24 hr. before test 3 oz. O. J. Total = 400 mg. i.m. and 3 oz. O. J. for 7 days (disp. patient).
7.	Before treatment	0.09	0.17	0.08	0.72	None.
	After 2 treatments	0.23	1.02	0.79	18	24 hr. before test 200 mg. i.m. Total = 400 mg.
8.	Before treatment	0.08	0.14	0.06	0.48	None.
	After 2 treatments	0.37	0.58	0.21	7.8	24 hr. before test 200 mg. i.m. Total = 400 mg.

TABLE VI—CONT'D

9.	Before treatment	Traces	0.10	0.10	0.10	None. Test Dose: 400 mg.
	After 3 treatments	0.42	0.57	0.15	6.3	24 hr. before test 200 mg. i.m. Total = 800 mg. Test dose now 200 mg.
10.	Before treatment	0.04	0.20	0.16	0.64	None.
	After full treatment	0.21	0.99	0.78	16	No vitamin C for 8 days before test. Total = 1000 mg.
13.	Before treatment	0.10	0.14	0.04	0.40	None.
	After 1 treatment	0.06	0.68	0.62	3.7	48 hr. before test 200 mg. i.m.
	After 3 treatments	0.55	0.86	0.31	17	24 hr. before test 200 mg. i.m. Total = 600 mg.
14.	Before treatment	Traces	0.16	0.16	0.16	None.
	After 1 treatment	0.10	0.34	0.24	2.4	24 hr. before test 200 mg. i.m.
	After 2 treatments	0.28	0.82	0.54	15	24 hr. before test 200 mg. i.m. Total = 400 mg.
	After 3 treatments	0.24	1.18	0.94	23	72 hr. before test 200 mg. i.m. None since. Total = 600 mg.
	After full treatment	0.61	1.19	0.58	35	24 hr. before test 2 oz. O. J. Total = 800 mg. i.m. and for 18 days 2 oz. O. J.
15.	Before treatment	Traces	0.15	0.15	0.15	None.
	After 3 treatments	0.51	0.77	0.26	13	24 hr. before test 200 mg. i.m. Total = 600 mg.
16.	Before treatment	0.13	0.17	0.04	0.52	None.
	After full treatment	0.73	1.54	0.81	59	24 hr. before test 200 mg. i.m. Total = 1600 mg.
17.	Before treatment	0.05	0.09	0.04	0.20	None
	After full treatment	0.44	1.33	0.89	39	24 hr. before test 2 oz. O. J. Total = 800 mg. i.m. and for 5 days 2 oz. O. J.
18.	Before treatment	0.04	0.07	0.03	0.12	None. 18 min. after injection plasma vitamin C = 3.22 mg. %.
	After 1 treatment	0.08	0.25	0.17	1.4	24 hr. before test 200 mg. i.m. 45 min. after injection plasma vitamin C = 1.56 mg. %.
	After 2 treatments	0.22	0.51	0.29	6.4	24 hr. before test 200 mg. i.m. Total = 400 mg.
19.	Before treatment	0.03	0.15	0.12	0.36	None
	After full treatment	0.24	1.25	1.01	24	48 hr. before test 1 oz. O. J. Total = 400 mg. i.m. and for 7 days 1 oz. O. J.

fact that the vitamin reserves of these two groups are of approximately similar magnitude. In 68 of 70 tests we obtained correct information by this test. This is 97 per cent compared with 91 per cent, when only the final plasma vitamin C was used as criterion.

Although the index thus seemed to be more satisfactory in our series, only time and accumulation of much greater material will establish definitely whether the additional labor of another venepuncture to determine the "initial value" is justified by a substantial gain in the accuracy of our measurement of vitamin C nutrition.

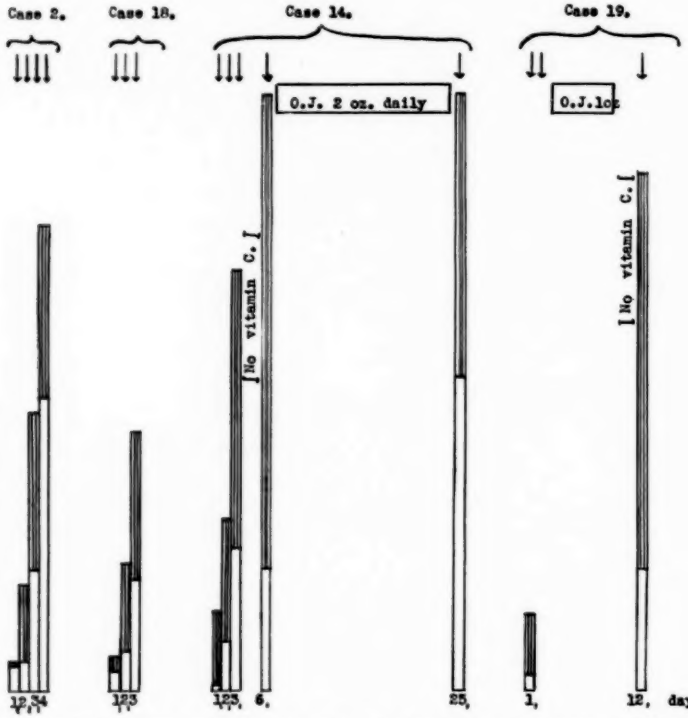

Fig. 3.—Illustrating the inadequacy of the ordinary plasma vitamin C determination in judging the process of recovery when the treatment is irregular. The unshaded part of the column represents the initial value; the total column, the final plasma concentration after injection; the arrows represent injections of 200 mg. of cevitamic acid.

Fig. 3 shows that, as one might expect, in patients receiving regular daily parenteral treatment (Cases 2 and 18) both the initial plasma level and the index show successive increases from day to day. Thus it would appear that either of these values would be adequate as a measure of the degree of depletion of depots. In irregularly treated patients (Case 14), on the other hand, the plasma level is practically

unpredictable, does not show the same successively increasing values and apparently has little or no virtue as a criterion of the vitamin C nutrition. In contrast with this, the *final* plasma concentrations and the indices do increase on successive occasions, even in the course of irregular treatments, and have considerable value as a criterion.

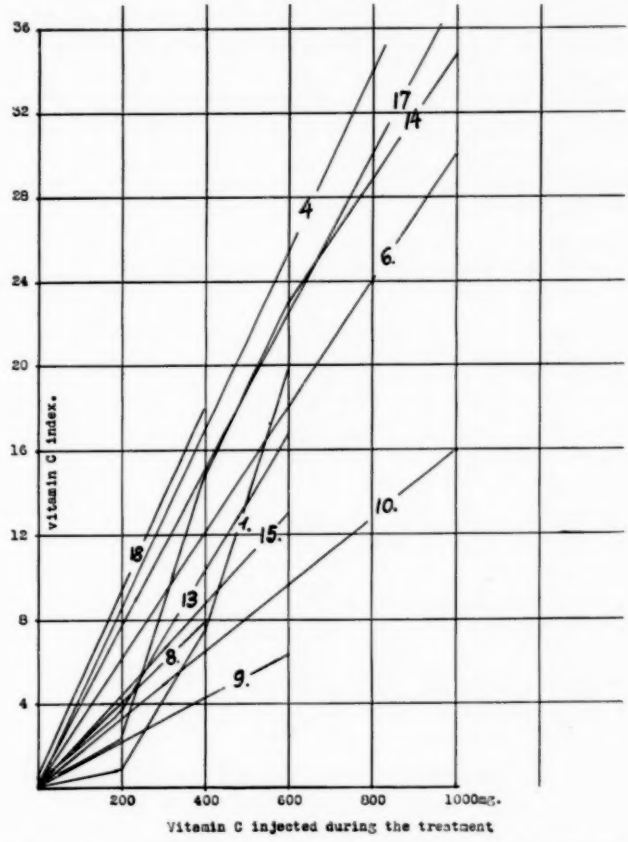

Fig. 4.—Illustrating the variability of the rate of recovery of the stores in different individuals.

COMMENTS

We should like to comment on two findings which have attracted our attention in this study. We have been struck by the variability of the recovery of the stores in different patients, quite apart from complicating infections. This is clearly shown in Fig. 4, where the results of the treatment are graphically represented. Since the treatment was altogether parenteral and hence differences in absorption do not enter into

consideration, it follows that such differences in the rate of recovery must be due to differences in the rate of utilization—in other words, the demand for the vitamin.

A second point which has impressed us has been the lack of correlation of the severity of the x-ray changes with the clinical and blood chemical findings; indeed, indices just as low were found in the x-ray negative cases of scurvy as in those with typical radiologic findings. This discrepancy is explained on the ground that the deficiency must be in operation for considerable time before recognizable x-ray changes will develop in the bones, and the presence of rickets may complicate the butic state; the x-ray changes give a rough indication of its *duration.* x-ray changes. The test measures the *severity* of the immediate scor-

SUMMARY

1. A review of the methods to determine the vitamin C nutrition is given; the applicability of parenteral "tolerance tests" to infants is established.

2. It is shown that, in estimating the vitamin C nutrition, the customary plasma vitamin C determination is not an adequate criterion.

3. The plasma vitamin C concentration four hours after the injection of the test dose is a better criterion. Values below 0.20 mg. per cent indicate scurvy, below 0.60 mg. per cent serious depletion of the depots.

4. In our series what we have called the vitamin C index seemed to be the most sensitive criterion. Our data are not numerous enough to establish rigid limits, but it seems that an index below 0.8 indicates clinical scurvy, indices between 0.8 and 6 indicate *very* deficient reserves. In normal subjects the index is usually well above 10.

5. It is pointed out that individuals appear to differ in their vitamin C requirements.

6. An explanation is offered for the discrepancy between the degree of the change noted in the x-ray of the bones and the clinical and blood chemical findings.

The authors are indebted to Dr. E. A. Park, Dr. L. E. Holt, Jr., and Dr. H. Josephs for their valuable suggestions and criticisms.

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COMPARISON OF THE VOLLMER TUBERCULIN PATCH TEST WITH PURIFIED PROTEIN DERIVATIVE

Results of Tests on 880 Rural School Children in St. Mary's County, Maryland

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THE technique of the tuberculin test has gone through various changes from the original von Pirquet, through the standardized intradermal test of Mantoux, to the use of purified protein derivative (abbreviated as PPD). Because of the stability of the latter product and accuracy of standardization, it has come into much favor. After extensive studies,[2] the National Tuberculosis Association has adopted the standard use of PPD, as the material most likely to give the highest number of reactors.* The first test dose represents 0.00002 mg. of PPD and the second 0.005 mg., 250 times as strong as the first. From comparative studies it appears that the first strength PPD will produce about as many reactors as 0.1 mg. of O.T. intradermally and the second strength as many as 1.0 mg. of O.T. Because of occasional severe reactions in sensitive individuals, the common procedure is to do a test with the first strength and follow with the second strength if the first is negative.

In addition to its value in establishing presence or absence of allergy to tuberculin in a given case, tuberculin testing has been thought to have a definite place as a case-finding procedure in public health work. The report of Lumsden, Dearing, and Brown[1] has thrown doubt on the accuracy of this method but no satisfactory substitute has been offered yet. Wholesale testing has been undertaken in St. Mary's County with the intention both of case finding and of stimulating the interest of a rural county which has a high mortality rate from the disease. During the course of the program, considerable data have been accumulated on the relative number of reactors to PPD and the Vollmer patch test. It is the purpose of this communication to report an analysis of these results merely as a comparison of the ability of the two tests to detect reactors, without entering into a discussion of the significance of a positive test.

St. Mary's County is the southernmost county on the western shore of Maryland with a population of approximately 16,000, of whom about 6,000 are colored. Last year there were sixteen persons who died of tuberculosis, nine of whom were colored, giving a total tuberculosis

From the St. Mary's County Health Office and the Bureau of Child Hygiene, Maryland State Department of Health.

*The assumption is made that there are no false positive reactions to carefully done tuberculin tests.

death rate of 105.2. It is interesting to note that in the total positive tests as described below, the positives among the white children were 35.2 per cent, and among the colored children 37.1 per cent, not unexpected figures in a county with such a high tuberculous mortality rate.

Doing a large number of intradermal tests requires considerable time, careful technique, and a good supply of needles. A disadvantage lies in the fact that the procedure is painful, even though only momentarily, and particularly in children, may be met with strenuous objections. This is further complicated by the necessity, in the usual procedure, of doing a second test on the large number negative to the first test.

The revival of interest in a test which does not involve breaking the skin, first introduced in 1907 by Moro, offered promise of a procedure which would overcome many of the objections to an intracutaneous test. No attempt will be made to review the stages in the development of this type of test, but the one introduced by Vollmer[4] appears to be superior from the standpoint of simplicity and accuracy of standardization. The test material consists of a strip of adhesive tape about 7.5 by 2.5 cm. on which are three 1 cm. squares of filter paper, the two outer ones saturated with old tuberculin, and the middle one, as a control, saturated with glycerin broth. It is recommended by Vollmer that the patch be applied to an area of skin which has been defatted with acetone or any other fat solvent. The sternum and anterior surface of the forearm are suggested as suitable locations. The adhesive is removed at the end of forty-eight hours and the test read twenty-four hours later. The latter interval is designed to obviate any confusion from reactions to the adhesive tape. If the test is positive there will appear under the patches of tuberculin, groups of tiny vesiculopapules. In a typical test there may be as many as fifty or seventy-five of these under each patch, while there are none under the control patch.

To date there have appeared three reports on the comparative accuracy of the patch test done by this method. All have been carried out on children who were known to be tuberculous. Vollmer and Goldberger,[4] testing 209 children, found a very high correlation between the patch test and the von Pirquet with agreement in 187 cases or 90 per cent. Where disagreement occurred the patch appeared to be more sensitive, since it was positive and the von Pirquet negative in fifteen cases or 7 per cent, with the reverse true in seven cases or 3 per cent. A second report by these same workers[5] emphasized that the test material was now more potent because of the use of O.T. prepared from growth on synthetic media. One hundred sixty-nine known tuberculous children were tested and there was perfect agreement between the patch and PPD I, except that the patch was positive in one case when PPD I was negative. PPD II was used in four cases and in one was positive when the patch was negative. In a group of 118 routine admissions to

Mt. Sinai Hospital in New York, eight children were positive to the patch and Pirquet, two positive patch and questionable Pirquet and two positive patch and Mantoux 1.0 mg. One hundred and six were negative to patch, Pirquet and Mantoux 1.0 mg.

Steward[3] using the test as described by Vollmer, examined 91 tuberculous children and five healthy adults. Ninety cases were positive to both the patch and the Mantoux test done with 0.1 mg. O.T. Six were positive to the patch but negative to the intradermal test.

The use of a tuberculin ointment patch test is reported on very favorably by Wolff and Hurwitz.[6] This differs from the Vollmer test in that the material used is a sterilized glycerin broth culture which has been concentrated and triturated. A "pea-sized drop" of the material is put on the skin and covered with adhesive tape. A control is used. The authors found 98.2 per cent agreement between this test and the Mantoux 0.1 mg. An obvious objection is the inaccuracy of a "pea-sized drop."

The present paper is concerned only with reporting the relative accuracy of the patch test measured against PPD, as found in the study to be described.

PROCEDURE

Over a period of two months 880 tuberculin tests have been done in St. Mary's County, including the total population of one private, two parochial, and four public schools. The age distribution extended from 5 to 21. PPD first dose and PPD second dose were injected intradermally, and the Vollmer patch test was applied to the skin after scrubbing it with acetone according to directions. Most of the latter tests were done by applying the patch longitudinally to the skin of the inner side of the forearm. On a few it was put across the forearm just below the elbow; no apparent difference was noticed between these locations. The standard for reading the intradermal tests was taken as an area of definite induration 5 by 5 mm., and the patch test was considered positive if there were, under the two patches of tuberculin, a total of at least five definite vesicles. The first dose PPD was injected and the patch test applied on Monday. The patch test was removed at the same time as PPD I was read on Wednesday. Those who were negative to PPD I were given PPD II on that day and the test read on Friday. The patch tests were observed on Thursday and Friday. In all cases where the patch test was positive, we found that it was as definite or even stronger on Friday than it was on Thursday, indicating that one may read the test forty-eight hours after removal of the adhesive just as well as after twenty-four.

In over twenty cases the patch test fell off or was removed by the child before forty-eight hours; these are not included in the total.

RESULTS

Of the 880 children tested, 483 were white and 397 colored. Although there were some differences between the races, the disparity was not enough to make it worth while to report the results separately. At least one of the three tests used was positive in 319 cases or 36.2 per cent of the total of 880.

Table I shows the relative number of positives for each test. PPD I and II are grouped together since it is assumed that any positive to PPD I will be positive to PPD II.

TABLE I

DISTRIBUTION, ACCORDING TO TESTS, OF THE 319 TOTAL POSITIVES OUT OF 880 CHILDREN TESTED

TEST	NUMBER POSITIVE	PER CENT OF ALL POSITIVES
PPD I	131	41.1
PPD I or II	319	100.0
Patch	94	29.4

It is obvious that the patch test was far inferior to PPD in detecting tuberculin reactors. It was not even as good as the first strength of PPD, even though, as appears in Table II, the patch test did pick up some reactors which were negative to PPD I. The superiority of PPD I over the patch is statistically significant, since the probability of such a difference occurring by chance is about 1 in 500.

TABLE II

CORRELATION OF THE PATCH AND PPD I AMONG THE 319 TOTAL POSITIVES

	PPD I POSITIVE	PPD I NEGATIVE	TOTAL
Patch positive	76	18	94
Patch negative	55	170	225
Total	131	188	319

The patch test, then, did pick up eighteen or 9.6 per cent of the 188 in which PPD I was negative. By contrast, however, PPD I detected fifty-five or 24.4 per cent of the 225 in which the patch was negative.

In order to check the influence of location on the usefulness of the patch test it was repeated in fifty-two children positive to PPD, who had given a negative patch test on the arm, applying the second patch test over the sternum. Only sixteen children of these fifty-two were positive with the repeated test. While this might indicate that the sternum is a better location than the arm, it would not affect the major results or conclusions. Besides, young ladies of high school age and over object to wearing the adhesive tape in so prominent a site.

It would seem to be clear that the patch alone cannot replace PPD either as a diagnosticum in the individual patient or as a case-finding procedure in public health work. Because of the obvious convenience

of the patch test, a possible field of usefulness suggests itself. One might employ the patch for the primary test in place of PPD I, recognizing that if the test is negative it must be followed by PPD II before a definite opinion can be given. Even here one must recall that the patch found many less reactors than PPD I, meaning that one would have to do more tests with PPD II than if PPD I were used for the preliminary test. Other factors, too, must be taken into consideration, such as relative expense and possible difficulties because of removal of the patch before the stated time.

Lumsden's work with regard to variability between the two brands of PPD on the market is very disconcerting and may play some role in explaining the discrepancy between our results and those of other investigations. In view of the fact, however, that all the previous papers on the patch test have been uniformly favorable, it has seemed important to us to put on record the present figures.

SUMMARY AND CONCLUSIONS

Eight hundred and eighty tuberculin tests were done on school children comparing the Vollmer patch test with the PPD intradermal test. The patch was found positive in only 30 per cent of the cases positive to PPD I or II. It is believed that this is sufficient evidence that a negative patch test does not by any means eliminate the possibility of a positive reaction to tuberculin and that the patch test alone is unsuitable as a screening method for finding the tuberculin reactors in a school population.

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A STUDY OF 1,852 CHEST ROENTGENOGRAMS OF TUBERCULOUS CONTACTS UNDER THE AGE OF FIVE YEARS

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THE value of roentgenographic examination in the diagnosis of pulmonary tuberculosis of the adult or reinfection type has been established by numerous studies, correlating the roentgen ray findings with clinical and necropsy data. The presence of abnormal areas of differing density, of shadows representing cavities, consolidation, fibrosis, and nodular infiltration is so characteristic that there is, in most cases, little question as to the true etiology. Questionable appearances may occur, and there are a number of conditions, notably neoplasms, mycotic infection of the lung, silicosis, anthracosis, and certain other conditions which may give rise to confusion, but in the vast majority of cases the skillful reading of a well-made roentgenogram of the chest gives reliable information of the presence and morphologic distribution of pulmonary tuberculosis of the adult type.

In the case of the primary infection (childhood type of tuberculosis), such as is usually encountered in the lungs of infants, school children, and adolescents, the diagnostic criteria in the roentgenogram are less firmly grounded. Not only are the tuberculous lesions found in this group less characteristic in their appearance, but acute pulmonary lesions of a nontuberculous nature are much more likely to confuse the picture. The elaborate classification of childhood type tuberculous lesions shown on the roentgenogram, as described by McPhedran,[1] characteristic lesions of which are frequently observed, is complicated by the presence of borderline and intermediate forms, as well as by the fact that pictures similar to those observed are also often seen in nontuberculous cases. The fact that tuberculous lesions are rarely present in children with negative tuberculin skin tests has led to a neglect in roentgenographing these children. There is a common tendency to interpret most pulmonary lesions seen on the roentgenogram in the cases of the children with positive tuberculin tests as if the lesion were necessarily resultant from the tuberculous infection. In a few series, such as those of Myers[2] in Minnesota, Pope,[3] and Lord[4] in Massachusetts, films taken of children of school age showed an absence or low incidence of pulmonary shadows in those with negative tuberculin tests as compared to those with positive tuberculin reactions.

During the first few years of life, however, insufficient attention has been given to the difficulty in the interpretation of the roentgenographic

From the Bureau of Laboratories, Department of Health.

shadows observed. Roentgenograms in infancy are usually taken because of some definite clinical indication, which frequently guides in their interpretation. Moreover, the technical difficulties of the roentgenographic examination of infants are great. The mobility of the body parts lead to abnormal temporary conformations. The great difficulty in orienting the infant on the film, the lessened density of the tissues, and the great differences in films due to slight variations in technique all add to the inaccuracies in the interpretation of the findings.

SUBJECTS AND METHODS

In the course of the investigation of immunization against tuberculosis with B.C.G. started in New York City in 1926, routine roentgenograms were taken of control children as well as vaccinated children. These routine roentgenograms furnished the material used in this study. All the children in this study were from homes where one or more members were tuberculous. Many of the children, however, were never exposed to open tuberculosis.

The material was obtained from (1) the children followed as controls in the B.C.G. investigation and (2) a group of children already infected when first seen by us and therefore not used as control cases in the B.C.G. study. The first group consists of children with persistently negative skin tests as well as those who later developed a positive tuberculin test. This report does not include infants who received B.C.G. vaccine, since the administration of the vaccine usually produces a temporary allergy to old tuberculin, and this precludes the use of this valuable criterion of tuberculous infection.

The ages of the children ranged from birth to 5 years. Most of the children were seen in the first year of life, but, since many children included in this study have not yet reached their fifth year, the number followed declined to about one-half at the fifth year. The sexes were almost evenly divided, and, since no significant differences between the sexes were observed in any of this work with infants, they will be considered together throughout the study.

The routine testing dose in this work is 0.1 to 0.2 mg. of old tuberculin. Many children, however, were tested with doses varying up to 5.0 mg. All children used as controls for the B.C.G. investigation either are known from birth or are under one year of age with a negative tuberculin skin test when accepted. About 20 per cent of those followed developed a positive Mantoux test during the first five years of life. Routine roentgenograms were taken not only of those children developing a positive Mantoux test, but also of those with persistently negative skin tests.

The group of cases who had positive Mantoux tests at the time of their first examination, although not used as controls in the B.C.G. study, were followed and investigated as closely as the other cases. These children, when referred for study, were regarded as healthy. Some of them

showed abnormal pulmonary shadows when first roentgenographed. The children were divided according to their exposure into known open or closed cases of tuberculosis. The effect of such exposure was noticeable on the frequency of infection, the incidence of the various roentgenographic findings observed, and the mortality from tuberculosis.

The films of the children were taken at various hospitals and clinics throughout the city. However, only those roentgenograms which could be secured for examination and reading were included in the study. The tuberculin test and clinical findings were not available to the reader of the films. Shadows in the films were not read as tuberculous, but were merely described.

Altogether 1,852 different films, representing 584 infants, were examined in this study. There was some variation in the frequency with which roentgenograms were taken. There were more roentgenograms taken of children with positive reactions and those exposed to open tuberculosis than of those in whom clinical infection was less likely.

RESULTS

Abnormal shadows of opacities were observed in 153 of the 584 infants roentgenographed, or 26 per cent of the total number. These abnormalities varied widely, both in character and extent. They may be readily divided into two main groups according to location as (1) tracheobronchial and (2) parenchymatous. The former includes shadows close to the mediastinum, such as are often interpreted as suggesting hilar, paratracheal, or peribronchial tuberculous lesions. The parenchymatous group consists of cases with shadows over what is generally considered as the normal lung field, such as are seen in pneumonia, parenchymal tuberculous lung lesions, or pleural lesions. Many of the films in the parenchymal group also showed an increase in tracheobronchial shadows. In this study such combinations of the two lesions are listed in the parenchymal group. This method of grouping the cases naturally tends to swell the number in the parenchymal group and diminish the number of cases with tracheobronchial shadows. It must also be remembered that this study permitted the examination of serial films on infants from early in their infection through the first few years of life. Consequently, many more parenchymal lesions were observed than one would ordinarily expect in a cross section roentgenographic study of a group of tuberculin-positive infants.

In the study of the available material comprising this investigation, the cases were considered according to their reactivity to tuberculin. The 127 infants with positive initial Mantoux tests were combined with the 78 who, though negative when first tested, subsequently became infected. The 379 persistently negative Mantoux cases comprise the other group.

Examination of the roentgenograms of the Mantoux-positive and Mantoux-negative reactors (Table II) shows that abnormal shadows were observed in 49.2 per cent of the former as compared with 13.6 per

cent of the Mantoux-negative group. The greatest difference was noted in the incidence of parenchymal lesions, where the ratio observed in the positive and negative reactors was about 5 to 1. The incidence of tracheobronchial shadows only showed little difference in the two groups. As previously noted, cases with tracheobronchial shadows, which at some time showed a parenchymal lesion, are listed only in the latter group. Because of the frequency with which roentgenograms were taken, parenchymal lesions were found more often than if fewer films were available. It would appear, however, that a diagnosis of tuberculosis of the tracheal or peribronchial glands may not be made from the roentgenogram alone, even in tuberculin-positive infants, unless definite calcification is seen. Even if correction is made for the occurrence of parenchymal shadows in the tuberculin-negative group, it might be inferred from our series that the great majority of the parenchymal shadows in the group of tuberculin-positive infants are caused by tuberculous lesions.

TABLE I

NUMBER OF ROENTGENOGRAMS OF CASES STUDIED

TYPE OF CASE	NUMBER ROENTGENOGRAPHED	NUMBER FILMS TAKEN	YEAR OF LIFE WHEN ROENTGENOGRAPHED				
			1	2	3	4	5
Subjects with persistently negative Mantoux test	379	989	261	163	127	90	61
Subjects who developed positive Mantoux test after admission to study	78	302	46	46	34	27	24
Subjects with positive Mantoux test when first examined	127	561	86	103	98	78	84
Total	584	1,852	393	312	259	195	169

TABLE II

FREQUENCY OF ABNORMAL ROENTGENOGRAMS

	NUMBER ROENTGENOGRAPHED	NUMBER WITH TRACHEOBRONCHIAL GLAND SHADOW ONLY		NUMBER WITH PARENCHYMAL SHADOWS		TOTAL	
Negative Mantoux cases	379	26	6.8%	26	6.8%	52	13.6%
Positive Mantoux cases	205	19	9.2%	82	40.0%	101	49.2%
Total	584	45	7.7%	108	18.4%	153	26.1%

Another approach to the problem of interpreting the specificity of roentgen shadows may be made by examination of later films in the cases that at one time showed a positive shadow. The use of serial roentgenograms of the same infant will often help to solve difficulties. Enlarged glands due to tuberculosis should generally appear similar on two closely

successive films, if the technique, exposure of the film, and position of the patient are approximately the same. Calcification should be constant in appearance, and parenchymal pulmonary lesions have a tendency to remain longer than most acute respiratory infections of the lung in childhood. The findings of the study of later films in cases with positive roentgenograms are shown in Table III. An arbitrary period of three months was selected as the minimum period for the persistence of roentgenographic shadows previously noted.

The number of cases is small since many children with positive roentgenograms were not re-examined sufficiently soon after the first film to permit careful observation of shadow changes. The disappearance of previous shadows was particularly marked among the cases with tracheobronchial shadows and negative Mantoux tests, 73.7 per cent disappearing within a period of three months. Among the positive Mantoux test cases, only 28.7 per cent of the tracheobronchial shadows disappeared during the same period of time. This lends support to the previous finding of the difficulty of interpreting the etiology of such shadows. Parenchymal shadows showed more persistence, only 7.6 per cent disappearing within three months in the positive Mantoux group, as against 50 per cent among the negative reactors. Although the possibility exists that

TABLE III

CHANGES IN ROENTGENOGRAMS

	TRACHEOBRONCHIAL GLAND SHADOWS				PARENCHYMAL SHADOW			
	PERSIST		DISAPPEAR		PERSIST		DISAPPEAR	
Negative Mantoux cases	4	26.6%	11	73.7%	8	50.0%	8	50.0%
Positive Mantoux cases	10	71.3%	4	28.7%	61	92.4%	5	7.6%
Total	14		15		69		13	

some of the lesions might have been tuberculous but actually disappeared in a short time, this does not appear to have been probable in most cases.

The possibility that some of the parenchymal shadows in the tuberculin-negative group were of tuberculous origin despite the absence of tuberculin allergy must also be considered. Although such a possibility may seem remote, a study of the eight cases with persistent negative reactions to as high as 5.0 mg. of tuberculin and persistent parenchymal shadows some of which eventually went on to calcification, suggests that these children may have had a tuberculin anergy. A detailed study of these cases will be the subject of a subsequent paper.

Among the 27 children who died of tuberculosis and who had been adequately roentgenographed, 26 (96.3 per cent) showed definite parenchymal shadows and one (3.7 per cent) showed a glandular type of lesion only. The lack of roentgenograms shortly before death in certain

other cases was due to the fact that the children were not in hospitals, and portable roentgenographic examination at their homes was not available in this study. Seven of the children had negative tuberculin tests. However, four of these were not tuberculin-tested for three or more months prior to their death. Tuberculin tests were generally not done more frequently than every three months in our series, unless the child was hospitalized. The remaining three with negative reactions were tested three, four, and five weeks before death. All had positive roentgenograms, and their anergy may be explained by the presence of an overwhelming infection. Fourteen post-mortem examinations were performed, and all demonstrated tuberculous lesions. In one of these cases the premortem diagnosis was nonspecific bronchopneumonia and alimentary intoxication. The post mortem of this child revealed tuberculosis with miliary dissemination.

SUMMARY

A study of 1,852 chest roentgenograms on 584 infants from tuberculous homes varying in age from birth to five years is presented.

Among 379 cases with negative Mantoux tests, the incidence of tracheobronchial shadows alone was 6.8 per cent. The incidence of parenchymal shadows was also 6.8 per cent.

Among 205 cases with positive Mantoux tests, the incidence of tracheobronchial shadows alone was 9.2 per cent; the incidence of parenchymal shadows was 40 per cent.

Increased tracheobronchial shadows persisted more than three months in 26.6 per cent of the negative Mantoux cases, as against 71.3 per cent of the tuberculin-positive cases.

Parenchymal shadows persisted on subsequent examination for three months or more in 8 of 16 (50 per cent) of the negative Mantoux cases, and in 61 of 66 (92.4 per cent) of positive tuberculin cases.

Infants dying of tuberculosis generally show demonstrable parenchymal shadows on a roentgenographic film. In our series, since miliary tuberculosis was the most frequent cause of death, the diagnosis of lethal forms of tuberculosis by roentgenographic examination was readily made.

Increased tracheobronchial shadows in infancy may not be accepted as pathognomonic of tuberculosis, even in the presence of a positive Mantoux test. It appears, however, that a great majority of the parenchymal lesions in tuberculin-positive infants are probably tuberculous in nature.

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THE VALUE OF ROENTGENOGRAPHIC EXAMINATION IN THE DIAGNOSIS OF SYPHILIS IN NEWBORN INFANTS

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THE difficulty of making a diagnosis of syphilis in the first few months of life is well known. In a previous report[1] the author has pointed out the importance of proper interpretation of the serologic test for syphilis in this early age period. A number of other investigators have advocated roentgenographic examination of the long bones as the best means for making an early diagnosis of syphilis in infants.

It is the purpose of this paper to point out certain difficulties in diagnosing syphilis by roentgenographic examination. Before setting forth the results of this study, the reports of other investigators will be briefly referred to, as follows:

McKelvey and Turner[2] made roentgenographic observations on the long bones of 229 newborn infants whose mothers were syphilitic. In 19 cases the roentgenograms showed evidence of syphilis in the infants, and all these infants developed clinical or serologic evidences of syphilis. Of the 210 infants with roentgenograms negative for syphilis 43 (21 per cent) ultimately developed evidences of syphilis. Parmelee and Halpern[3] in a clinical, serologic, and roentgenographic study, pointed out "the predominant importance of the roentgenologic evidence of osseous syphilis in the diagnosis of congenital syphilis during early infancy." In a series of 79 infants born of syphilitic mothers and studied in the first few days of life there was suggestive clinical evidence of syphilitic infection in 19 per cent, serologic evidence in 23 per cent, and roentgenographic evidence in 44 per cent of the cases. Ingraham,[4] in a study of the early diagnosis of syphilis in the "period of doubt," found roentgenographic evidence of syphilis in 29 per cent of a series of 127 newborn infants born of syphilitic mothers. He stated that "this represents a little more than half the cases which became subsequently positive to this type of investigation." In a later study of roentgenographic methods of diagnosis, Ingraham[5] found that 19 per cent of the infants studied had changes in their long bones which made possible a diagnosis of syphilis before the sixth day of life. In all these latter cases the roentgenographic changes were present before serologic examinations were of value in establishing a diagnosis.

METHOD AND SCOPE OF STUDY

This study is based on 83 infants who were born of syphilitic mothers, the diagnosis of syphilis in the mothers having been established by one or several positive Wassermann reactions. The amount of treatment

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given to each mother was known, the cord Wassermann tests had been positive, and roentgenograms of the long bones of each infant had been made during the first 10 days of life. Each of the 83 infants was followed clinically and serologically until such time as he was considered to be proved syphilitic or nonsyphilitic. If an infant was considered syphilitic, treatment was instituted; if nonsyphilitic, his blood was tested at intervals for at least one year.

The roentgenograms of the long bones were read at the Department of Roentgenology of the Johns Hopkins Hospital* and recorded as negative, positive, or "doubtful" without knowledge of the mother's history in regard to treatment, the results of serologic tests, or the outcome of the clinical and serologic follow-up of the infant.

TABLE I

RESULT OF ROENTGENOGRAPHIC EXAMINATION AND OF FOLLOW-UP SEROLOGIC TEST

ROENTGENOGRAPHIC EXAMINATION	TOTAL	FOLLOW-UP SEROLOGIC TEST	
		NEGATIVE	POSITIVE
Total	83	68	15
Negative	57	47	10
Positive	3	1	2
"Doubtful"	23	20	3

RESULTS OF ROENTGENOGRAPHIC EXAMINATIONS

The results of the roentgenographic examinations and of the serologic tests are shown in Table I.

Of the roentgenographic examinations of the long bones made within 10 days of birth of the 83 infants born of syphilitic mothers, 57 were recorded as negative, 3 as positive, and 23 as "doubtful."

Of the 57 infants with a negative roentgenographic diagnosis, 10 subsequently developed clinical and serologic evidences of syphilis; 47 did not.

Of the 3 infants with positive roentgenographic diagnoses, 2 developed clinical and serologic evidences of syphilis; 1 did not.

Of the 23 infants with "doubtful" roentgenographic diagnoses, 3 developed clinical and serologic evidences of syphilis; 20 did not.

As a result of the follow-up studies of these infants it is evident that the roentgenographic examination was of value in establishing an early diagnosis of syphilis in but 2 of the 83 infants studied. The roentgenographic examination correctly established a diagnosis of "no syphilis" in 47 of the 57 infants. For the 23 infants with "doubtful" roentgenographic diagnoses the roentgenographic examination obviously did not establish a definite diagnosis.

The group of 23 infants for whom the roentgenographic diagnosis was "doubtful" is worthy of special comment, because some of the changes

*The author wishes to express his appreciation of the assistance of Dr. J. William Pierson, associate professor of roentgenology, Johns Hopkins Hospital. Dr. Pierson has pointed out that in the evaluation of the roentgenograms at the Johns Hopkins Hospital the term "doubtful" was used arbitrarily to indicate that the roentgenogram showed some variation from the normal, however slight, the exact significance of which was not entirely clear.

found in the roentgenograms which were suggestive of syphilis were shown to be due to causes other than syphilis; for example, deposition of bismuth in the bones of the fetus as a result of treatment of the mother, severe illness of the mother, or rapid growth of the infant after birth.

Bismuth Lines.—Caffey[6] has shown that treatment of pregnant women with bismuth brings about changes in the bones of the fetuses, described by him as "heavy transverse bands of increased density at the ends of the shafts." Some investigators have confused these changes with changes due to syphilis, probably because the density of the bands gives an appearance of rarefaction proximal or distal to them similar to that seen in syphilis. McLean[7] states that "in fetuses, as well as in infants in the first weeks of life, a deepening in the longitudinal axis of the provisional zone of calcification of the long bones, shown on the roentgenogram as a white cap on the diaphyses and on the positive print as a dark metaphyseal band" has been usually considered evidence of syphilis. He points out that "the roentgenologist should be cautious about making a diagnosis of syphilis on this evidence alone. . . ."

Of the 83 infants in this study, there were 73 whose mothers had received bismuth injections during pregnancy. In 22 of these cases a "doubtful" diagnosis of syphilis was made by roentgenogram. In the 10 cases in which the mothers had not received any treatment with bismuth, there was only one "doubtful" diagnosis of syphilis.

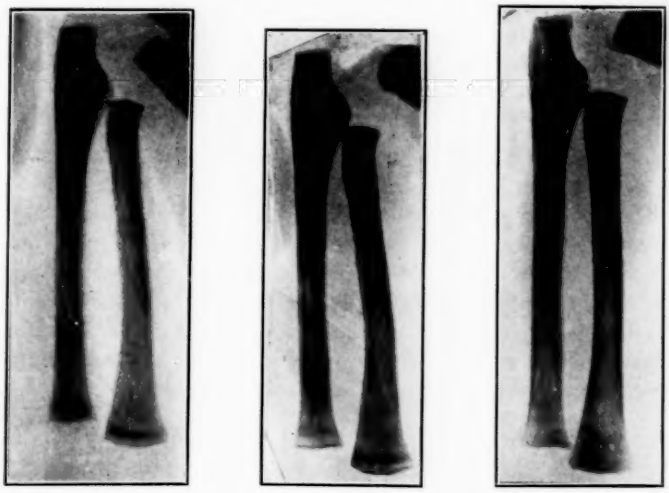
The following case histories give examples of the occurrence of bismuth lines in the bones of nonsyphilitic infants.

CASE 1.—Baby B. B. The mother reported for prenatal care Sept. 23, 1936. The mother's Wassermann reaction was found to be positive, and antisyphilitic treatment was begun Sept. 25, 1936. Between this time and Oct. 28, 1936, when the infant was born at term, the mother received 0.8 gm. of bismuth, 0.6 gm. of neoarsphenamine and 2.5 gm. of arsphenamine.

Roentgenograms of the infant's long bones were made on the second day of life. Fig. 1*A* shows a thin line of density at the extreme distal end of both radius and ulna, proximal to which are first a zone of rarefaction, then a broader dense band, and then another zone of rarefaction. In this case the roentgenographic diagnosis was recorded as "doubtful." The infant, however, at that time did not have clinical manifestations of syphilis and did not develop them, although no treatment for syphilis was given. The reaction to the quantitative Wassermann tests became progressively weaker until on the seventy-sixth day of life it was negative. A test made on the one hundred and twenty-fifth day of life was also negative. Additional roentgenograms were made at 2 weeks of age (Fig. 1*B*) and at 2 months (Fig. 1*C*). The bands of density that appear in Fig. 1*A* appear also in Figs. 1*B* and 1*C*. In Fig. 1*C*, the latest roentgenogram made, the bands are less marked than in the two earlier ones.

These bands of density were considered to be due to deposition of bismuth in the bones of the infant.

CASE 2.—Baby A. F. The mother of this infant had been given 1.6 gm. of bismuth intramuscularly in eight weekly injections. She had not received vitamin D in addition to her usual diet. The bismuth had been readily absorbed, and there were no local nor general signs of toxicity from the drug. At the end of the two hundred



A. *B.* *C.*

Fig. 1.—Case 1. *A.* Roentgenogram made on second day of life shows a thin line of density present at the distal end of both radius and ulna, proximal to which is a zone of rarefaction and then a broader zone of increased density.

B. Roentgenogram made at 2 weeks of age shows the bands of density the same as in Fig. 1*A*.

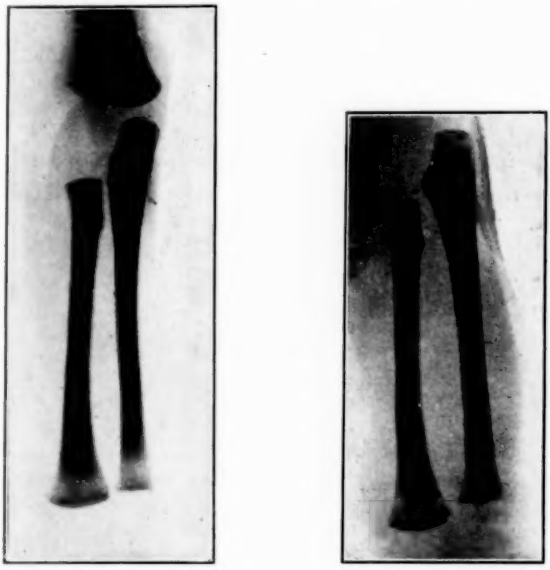
C. Roentgenogram made at 2 months of age shows the bands still present but less dense.

Fig. 2.—Case 2. Roentgenogram of the radius and ulna made on the seventh day of life shows dense bands at the ends of both radius and ulna, with a zone of rarefaction between them.

and seventy-sixth day of pregnancy a full-term infant weighing 3,750 grams was born spontaneously. The Wassermann reactions of both mother and infant were negative following delivery. A roentgenogram of the infant's long bones, made on the seventh day of life (Fig. 2), showed essentially the same type of dense bands at the end of both radius and ulna as those shown in Fig. 1.

As in Case 1, the bands were considered to be due to deposition of bismuth.

Zones of Submetaphyseal Rarefaction.—Another change in the long bones observed was submetaphyseal rarefaction which has been described by others as pathognomonic of syphilis. McLean[7] has stated, however, that "a very slight or very marked degree of submetaphyseal rarefaction, either with or without the deepened provisional zone of calcification," seen in roentgenograms of the long bones made in the first months of life is usually pathognomonic of syphilis, but does occur occasionally in other conditions. The following case shows that these changes may occur in a nonsyphilitic infant who is growing rapidly.



A. *B.*

Fig. 3.—Case 3. *A*, Roentgenogram of the radius and ulna made on the nineteenth day of life shows rarefaction in the submetaphyseal region.

B, Roentgenogram made at six weeks of age shows the same appearance of rarefaction, which is less marked than in Fig. 3*A*.

CASE 3.—Baby L. B. After the mother had been ill for six weeks her pregnancy was interrupted by cesarean section about five and one-half weeks before term. The weight of the infant was 2,410 grams and the crown-heel length was 46.5 centimeters. Roentgenograms, made shortly after birth, of the infant's long bones were considered to show no evidence of syphilis. Two Wassermann tests had been made of the mother's blood; the reaction to each was negative, as was that of the cord blood.

Following an initial weight loss of 270 grams the infant began to gain regularly on a whole-milk mixture (28 calories to the ounce) and weighed 2,460 grams on the nineteenth day of life. A roentgenogram of the long bones made on this day was reported to show rarefaction in the submetaphyseal region of all the long bones, such as is considered pathognomonic of syphilis (Fig. 3*A*). These findings were still present at 6 weeks of age, although not nearly so marked (Fig. 3*B*). The infant's Wassermann reaction was negative at 1 month of age and also at 3 and 6 months of age. At the age of 9 months the infant was living and well with no clinical evidences of syphilis.

The rarefaction shown in the roentgenograms was considered to be the effect, either direct or indirect, of the illness of the mother.

Cortical Shadows.—Periostitis has been generally recognized as one of the characteristic bone changes in syphilis in infancy. McLean[7] has pointed out that syphilitic periostitis seldom appears without other evidences of the disease in the bones. He states that "if any lesion of the cortex can be demonstrated by x-rays under the periosteal cloaking, the lesion can be said to be syphilitic." He points out, however, that "rapidly growing normal infants in the first months of life may show a fine periosteal shadow on the mesial aspect of the tibia," which may be mistaken for a pathologic lesion.

In the present study periosteal shadows, with and without other changes, have been seen frequently in normal, rapidly growing infants. These shadows have been seen not only in the tibia, but in other long bones as well. The following case history gives an example of cortical shadows in the bones of a nonsyphilitic infant.

CASE 4.—Baby H. H. After a normal pregnancy, the mother, a 14-year-old colored girl, gave birth to a female infant weighing 1,315 grams and measuring 36 centimeters in length. A Wassermann test was made of the mother's blood and of the infant's; in both cases the reaction was negative, as was that of the cord blood.

The infant was vigorous and gained rapidly, weighing 2,880 grams on the eighty-third day of life. She was fed artificially with a cow's-milk mixture, and after the first 2 weeks of life was given daily 1 ounce of orange juice, 30 drops of viosterol, and 5 c.c. of ferric ammonium citrate solution. The infant developed no clinical manifestations of syphilis.

Roentgenograms made of the long bones of the extremities, when the infant was 2 days old, revealed nothing abnormal. Additional roentgenograms, made at 35, 83, and 100 days, showed thickening of the cortex, or lamellation, best seen in the roentgenogram of the femur that was made on the thirty-fifth day of life (Fig. 4*A*). This lamellation is even more marked in subsequent roentgenograms (Figs. 4*B* and 4*C*). It is regular and symmetrical and extends over nearly the entire length of the bones. The tibiae and humeri showed the same type of change. This change might have been interpreted as syphilitic periostitis but was thought not to be evidence of syphilis because of its symmetry and the absence of other roentgenographic evidence of syphilis in the bones.

In these roentgenograms a fine line of increased density at the metaphysis was also present, as shown in Fig. 4*A*. This line has been described by McLean[7] as evidence of early syphilitic osteochondritis. He has stressed the point, however, that caution should be exercised in making a diagnosis of syphilis from this sign alone. Caffey[6] has observed in newborn infants who are not syphilitic "narrow and fine transverse lines."

A.

B.

Fig. 4.—Case 4. *A.* Roentgenogram of the bones of the lower extremity made on the thirty-fifth day of life shows lamellation of the cortex which is particularly marked in the femur. There is also a fine line of increased density present at the metaphysis especially marked in the fibula.

B. Roentgenogram made at 83 days shows more marked lamellation of the cortex of the femur.

C. Roentgenogram made at 100 days shows the lamellation is still present.

The periosteal changes shown in these roentgenograms were considered to be due to the rapid growth of the infant.

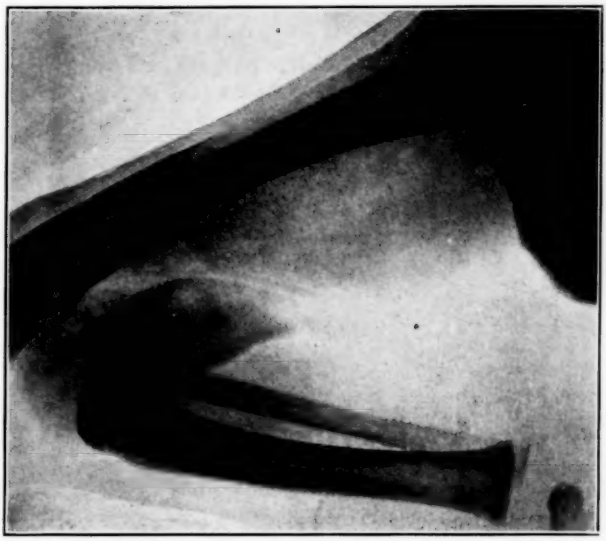


Fig. 4C.—(*See legend on page* 236.)

SUMMARY AND CONCLUSIONS

Eighty-three infants born of syphilitic mothers were studied by roentgenographic examination of the long bones in an effort to determine the value of this method of examination in the early and accurate diagnosis of congenital syphilis.

A diagnosis of syphilis, later shown by clinical and serologic follow-up to be correct, was made early in only 2 cases. In 47 cases a diagnosis of "no syphilis" was made, which was later shown to be correct. In 23 cases the diagnosis was recorded as "doubtful." The roentgenograms were of value in making a correct diagnosis in 49 cases.

Since conditions other than syphilis may bring about changes in the bones apparent in roentgenograms, it is advisable to confirm the roentgenographic findings by clinical or serologic examinations before a definite diagnosis of syphilis is made and treatment for the disease is instituted.

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II. TREATMENT OF SCARLET FEVER WITH SPECIFIC ANTITOXINS OF LOW PROTEIN CONTENT

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THE results obtained following the use of a concentrated scarlet fever antitoxin have been previously reported.[1] Towards the completion of that report, the authors began to evaluate another antitoxin which at that time had just been manufactured by Parke, Davis and Company. The latter antitoxin is refined and concentrated to contain the requisite number of units in the small volume of 3.2 and 3.5 cm.

Serum sickness commonly occurred following the administration of "unconcentrated" scarlet fever antitoxins previously used, the reaction rate being at least 38.5 per cent.[2] Others have reported rates ranging from 34.5 per cent to 38.9 per cent.[3] Following the use of one of the recently introduced antitoxins, the reaction rate was a little more than 11 per cent—a marked reduction in serum sickness.[1]

The purpose of this study was to determine (1) if there were fewer reactions following the use of this antitoxin than following the use of the previous material manufactured and sold by Parke, Davis and Company, and (2) if the scarlet fever antitoxin manufactured by them was as good as the antitoxins described in a recent article.[1]

Six hundred cases of scarlet fever were treated with this new antitoxin which was injected intramuscularly in all instances. Since the principal object of evaluating this antitoxin was to observe serum reactions, only one ampoule containing 6,000 units of scarlet fever antitoxin was injected in each patient, even in patients who might have shown better clinical improvement if 2 ampoules had been used. Five hundred cases of scarlet fever so treated have been analyzed and are the subject of this report.

Preliminary experiments were made with old antitoxins (not processed by the new method) of the same manufacturer and obtained in the open market. There were 3 such lots—numbers 034950K, 041775B, and 037985X. There were 8 reactions among 23 patients treated with the first lot, 2 among 10 treated with the second lot and 28 among 54 treated with the third lot of antitoxin. Thus, 87 patients were treated and 38 or 43.6 per cent had serum reactions.

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Three lots of scarlet fever antitoxins (numbers 096589A, 096619A, and 096619B), refined and concentrated according to new methods, were used. The latter 2 lots were obtained from the same pool, so that actually only 2 lots were tested. Fortuitous immunization of single animals may occur, in which event an antibody response of high titer may be obtained in one horse. This possibility was avoided, since antitoxins 096589A, 096619A and 096619B each contained the pooled serums of several horses.

Of the 500 cases injected, there were 11 serum reactions among those treated with antitoxin 096589A and 39 among those treated with 096619A and 096619B, a reaction rate of only 10 per cent. Serum sickness may be immediate, accelerated, or late, outlined as follows:

CLASSIFICATION OF SERUM REACTIONS

I. "*Immediate*" reactions are symptoms or signs which develop immediately or within 1 or 2 hours after the injection of the antitoxin. These are: (1) fever with chills, (2) pulmonary edema, (3) respiratory difficulties, (4) generalized itching, (5) generalized urticaria, (6) nausea and emesis. Any of the conditions mentioned may be associated with convulsions, sneezing, gastrointestinal symptoms, unconsciousness, arthritis or adenitis.

II. "*Accelerated*" reactions are symptoms and signs the same as listed under "immediate" and "late" reactions. The only difference is that the reactions in this instance come on within 2 to 3, and 24 hours after the use of an antitoxin.

III. "*Late*" reactions are symptoms or signs developing from 24 hours to a few weeks after the administration of antitoxin. These are generalized urticaria alone or with (1) arthritis, (2) adenitis, and (3) gastrointestinal symptoms.

Table I gives a summary of the number of each type of reaction. The results of the intradermal sensitivity tests are also included.

TABLE I

SERUM REACTIONS (50 TREATED PATIENTS WITH SCARLET FEVER)

TOTAL NO. OF CASES	INTRADERMAL SENSITIVITY	REACTIONS					
		IMMEDIATE	ACCELERATED	LATE		LOCAL AND GENERAL	IMMEDIATE AND LATE
				LOCAL	GENERAL		
50	Negative 18	0	4(1?)	4	10	0	0
	Positive 24	0	1	1	18	3*	1
	Not tested 8	0	0	0	7	1	0

*One patient had an Arthus phenomenon.

The antitoxin was blamed for anything that even closely resembled a serum reaction. Five patients who merely had a local urticaria about the intradermal sensitivity test made with the antitoxin were included with those who had serum sickness. None of the patients had immediate serum reactions. There were only 5 accelerated reactions (1 of which was questionable), a rate of only 0.1 per cent. There were 40 late reactions (only 8 per cent). The type of urticaria was not so severe as that seen with the administration of previous antitoxins in that

it did not last so long, and the symptoms were not severe. In only 2 instances was it present for more than 2 days; only 1 case had a recurrent attack of urticaria.

All of the 500 cases were given antitoxin on admission to the hospital. Three hundred and forty-seven or 69.4 per cent were moderately or severely ill and seemed to need some form of therapeutic treatment, while 153 or 30.6 per cent were not very ill (Table II).

TABLE II

RESULTS IN 500 TREATED PATIENTS WITH SCARLET FEVER

	NO. OF CASES	RESULTS				
		FAIR TO EXCELLENT	SLIGHT BENEFIT	FAIR TO GOOD BUT WITH FEVER RELAPSE	NO DEFINITE BENEFIT	QUESTIONABLE
Antitoxin 096589A						
Moderately to severely ill	52	31	2	7	9	3
Not very ill on admission	26	0	0	0	26	0
Antitoxin 096619A						
Moderately to severely ill	57	36	1	1	16	3
Not very ill on admission	28	0	0	0	25	3
Antitoxin 096619B						
Moderately to severely ill	238	159	31	18	27	3
Not very ill on admission	99	0	0	0	99	0
	Combined Results—Antitoxins 096589A, 096619A, 096619B					
Moderately to severely ill	347	226	34	26	52	9
Not very ill on admission	153	0	0	0	150	3

The criterion by which it was determined whether a patient had benefited from the antitoxin was severe. In order that a case could be classified as one having shown improvement, the temperature and pulse had to come down to normal within 12 hours to 24 hours. The striking subjective changes of improvement were ignored, since they could not be measured objectively. Subjectively, the patient might be clinically better after having received antitoxin, and yet he might have a fever which continued because of a local infection in the sinuses or ears. Although the results were obvious even under these conditions, the antitoxin was not credited with any beneficial results. It was felt that there should be objective evidence in order to demonstrate any clinical benefit.

Of the moderately to severely ill patients, 260 or 74.9 per cent showed some appreciable improvement (Table II). A chart illustrates the

marked beneficial results seen in some cases following the injection of the antitoxin (Fig. 1). Twenty-six patients (7.4 per cent) likewise had immediate beneficial responses, but in a few days they had fever relapses, i.e., the temperature rose again (Table II). These were not treated again, since the effect of only 1 ampoule of antitoxin was being investigated at this time. In clinical practice, however, 2 ampoules

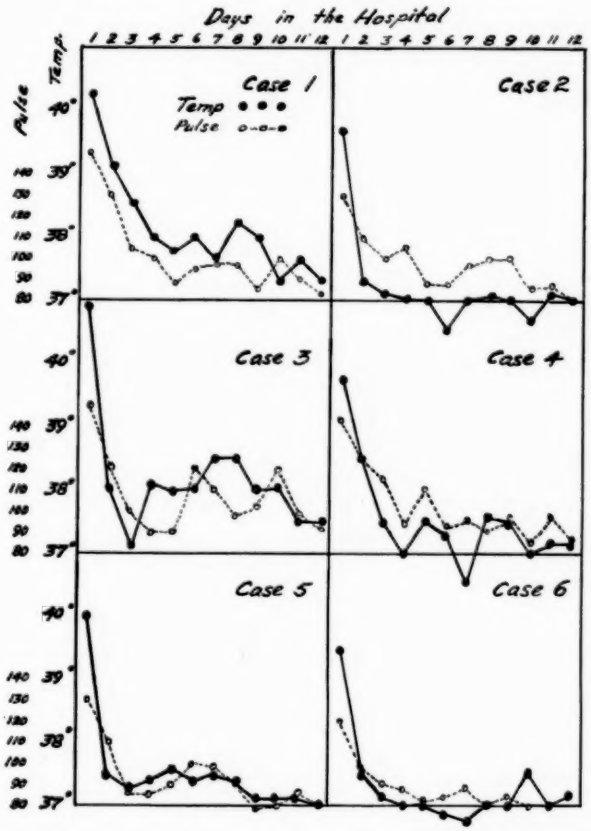

Fig. 1.—The temperature and pulse of 6 patients given antitoxin on the first day.

would have been given and the relapses of fever probably would have been fewer in number. Thus, 82.4 per cent of the moderately to severely ill patients were benefited. Fifty-two (14.9 per cent) were not benefited (Table II). The majority of these were admitted late in the course of the disease and usually presented some complicating factor which accounted for the fever.

Whether the patient that is not ill when first seen should be treated routinely is a question that cannot be answered at this time. However, it is the opinion of the authors that since the serum reaction rate is so low, the reactions so mild in character, and the complications which follow the use of these antitoxins minor and almost negligible, routine treatment might be given to every patient, the earlier the better.

TABLE III

COMPLICATIONS AND OTHER PATHOLOGIC CONDITIONS IN 500 TREATED PATIENTS WITH SCARLET FEVER

	EARLY	LATE		EARLY	LATE
Acne vulgaris	1	0	Influenza	0	3
Adenitis	269	23	Laceration		
Anemia, secondary	1	2	Legs	1	0
Appendicitis	1	1	Scalp	2	0
Arthritis	0	1	Lung		
Burns, second and third degree	3	0	Bronchitis	2	1
Cellulitis	1	0	Empyema (1 operated)	1	1
Conjunctivitis	11	0	Pneumonia		
Cyst, sebaceous	1	0	Bronchial	0	1
Cystitis, lachrymal	0	1	Lobar	1	1
Delivery, normal	1	0	Tuberculosis		
Diarrhea	2	1	Childhood type	1	0
Diphtheria	1	0	Pulmonary	3	0
Klebs-Löffler bacilli present without clinical symptoms	1	0	Mastoiditis (Early, 1 operated; Late, 5 operated)	5	8
Epistaxis	0	1	Myositis	1	0
Erysipelas	0	1	Nephritis	2	2
Glycosuria, renal	0	1	Otitis media	61	27
Heart disease			Paronychia	6	0
Early type (?)	1	0	Pyelitis	2	5
Congenital	1	0	Quinsy	3	1
Rheumatic	1	0	Rash (due to prontylin)	1	0
Heart, functional murmur	1	0	Reaction to blood transfusion	1	0
Hernia (1 operated)	2	0	Scarlet fever, second attack	0	2
Herpes	0	2	Sinusitis	20	14
Hordeolum	0	2	Smallpox vaccination reaction	0	5
Impetigo	1	1	Tinea capitis	2	0
Infected knee (ankylosed later)	1	0	Upper respiratory passages Nasal, tonsillar, pharyngeal, laryngeal areas inflamed and edematous	16	7
Infected wound of finger or toe	2	0	Vaginitis, nonspecific	0	1

Eight patients or 1.6 per cent died. This low mortality rate resulted in part from the wide use of sulfanilamide when late secondary complications appeared. It is the authors' experience, however, that this drug does not affect the early manifestations of scarlet fever, although it does help combat the later septic infections. Five of the 8 patients who died were admitted in a moribund condition. One patient was

a 24-year-old female with a post-Parkinsonian syndrome and bulbar involvement, a chronic dislocated jaw, an infected dermatophytosis, decubiti and edema of the glottis, and cervical lymphadenitis. She responded well to the antitoxin and became better from the scarlet fever, but died from the bulbar involvement 17 days after admission. She and the 5 who died within 24 hours after entrance to the hospital could not be classified as failures following any line of therapy. Nevertheless, they have been included in the total mortality rate and charged against the antitoxin. Ignoring these 6 cases, there were 2 deaths among 494 treated cases—actually a mortality rate of only 0.4 per cent, and this in a hospital to which are admitted the most severely ill patients of the community.

Of the 8 patients who died, 4 had been ill for more than 6 days before coming to the hospital; 2 were ill for 2 days before admission, 1 of the latter being the Parkinsonian case referred to, and the other, a case with a massive postoperative infection, cellulitis, septicemia, etc. The remaining 2 were ill 4 days before admission; 1 was a case of chronic alcoholism with delirium tremens and bronchopneumonia, and the other, a 4-year-old child with bronchopneumonia.

The complications or other clinical conditions found are enumerated in Table III. Some cases had multiple complications. Many of the latter, such as paronychia, etc., were of minor character and many too, though occurring during the course of scarlet fever, could not be attributed to the disease. Eighty-six of 524 cases treated with another concentrated antitoxin had complications, a complication rate of 16.4 per cent.[1] In this series, 80 of 500 or 16 per cent developed complications peculiar to scarlet fever. Many of them appeared late in the course of the disease, i.e., after the fifth day; some of these were merely extensions of involvements present on admission to the hospital. Six of the 23 late cases of marked adenitis and 5 of the late 27 cases of otitis media had these conditions on admission to the hospital. Epistaxis, influenza, cross infections, etc. could hardly be attributed to scarlet fever, but they are mentioned merely to complete the picture. One would like to know whether complications due to the disease were many and severe. There were 8 patients with late cases of mastoiditis (5 operated upon), 2 early and 2 late cases of nephritis, and 2 cases of empyema, one patient of which had a rib resection and had actually been admitted late in the course of the disease. One patient had an infected knee which later became ankylosed. There were 2 second attacks of scarlet fever and 1 case of arthritis. Two hundred and sixty-nine of the patients had palpable glandular enlargement on admission, but not large enough to be considered a complication. Sixty-one had otitis media; a common complication seen at the height of the disease. When the remaining complications as listed in Table III are studied, the impression is gained that these were such conditions as might occur in a

comparable group of 500 supposedly normal people. There were control cases, and though not a comparable number, it is, nevertheless, the opinion of the authors that the administration of both this and a previous antitoxin described[1] has decreased the number and severity of complications. The complication rate of 16 per cent with the use of concentrated antitoxin does not seem to be much of a reduction, until the types of complications in the untreated series are compared with the treated. There were 39 cases of nephritis, 3 cases of uremia, 3 cases of encephalitis, etc., as compared to few or none in the present treated series.

Some authors mention the appearance and disappearance of the rash as an indication of efficiency of a specific therapy. Such evidence is difficult to evaluate when it is noted that the hospital admission date does not in any way correspond to the date when the rash began. Nevertheless, the effect of the antitoxin on the rash was striking. In most instances, it disappeared or at least was greatly modified within 12 to 24 hours after the injection of the antitoxin. In most instances, likewise, there was no desquamation in these treated cases.

CONCLUSION

A new type of concentrated scarlet fever antitoxin has been used in the treatment of over 500 cases of scarlet fever. The results indicate that after the use of this antitoxin, the temperature fell rapidly, complications were probably decreased in number and severity, and the rash disappeared quickly; often, desquamation did not occur and serum reactions were low in number and mild in character.

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CONTROL OF COMMON CONTAGIOUS DISEASES IN PEDIATRIC WARDS OF A GENERAL HOSPITAL

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THE study divides itself into three parts: first, a review of the problem itself; second, a survey of the customary methods of meeting the problem and their advantages and disadvantages; and third, an outline of the proposed solution with an appraisal of its results.

I. REVIEW OF PROBLEM

For the purpose of this study those diseases customarily considered as the common contagious diseases, i.e., chicken pox, diphtheria, German measles, measles, mumps, scarlet fever, and whooping cough are the only diseases considered. Such communicable but not generally highly contagious diseases as the enteric fevers and sporadic meningitides, poliomyelitis, or encephalitis are not usually considered as requiring absolute quarantine and hence are not within the scope of this survey. The present rarity of smallpox permits its exclusion.

The control of these common contagious diseases can be readily reduced to three independent steps: first, the prevention of the admission to the pediatric wards of patients demonstrating these diseases in a recognizable form; second, the handling of such cases admitted during the incubation period of any of these diseases; and third, the disposal of cases which have resulted from the failure to control either of these first two steps and the prevention of secondary cases from these.

II. SURVEY OF CUSTOMARY METHODS OF MEETING THIS PROBLEM

Obviously considerable variation exists in the methods of handling these three phases of the problem in different general hospitals, but taken on an average a plan of the following type is most commonly employed:

A. *Admission of Contagious Cases.*—Varying degrees of caution are exerted in this regard, the least careful procedure permitting admission of all patients directly to the wards before examination, and the most cautious requiring examination by the admitting intern with a check of suspicious cases by a resident or visiting physician before admission. Obviously any plan which fails to fix the responsibility for examination and admission upon one man (preferably the admitting officer who is to

From the Department of Pediatrics of the Hahnemann Medical College and Hospital of Philadelphia, Pa., with the cooperation of the Department of Public Health of the City of Philadelphia, Pa.

The immune globulin (human) used in this clinical experiment was supplied through the courtesy of Sharp and Dohme, Philadelphia.

Presented before the Philadelphia Pediatric Society, Feb. 14, 1939.

take care of the case in the ward), one which permits even a few of the patients (such as ambulance cases or emergencies) to enter the wards without examination, or one which fails to provide ample opportunity for the examining intern to secure readily the collaboration of a more experienced physician, when desired, is certain to permit all too many cases of contagious disease to enter directly into the pediatric wards.

B. *Handling of Cases During Incubation Period.*—In general, the only attempt made to control this phase of the problem is to require the isolation of all admitted patients for varying periods. Ideally, of course, the isolation period should extend throughout the longest probable incubation period, or about 21 days, but, since the average pediatric ward in a general hospital has only from 5 to 50 beds, various compromises with this ideal have been necessary. It is safe to say that very few such hospitals isolate their newly admitted patients for more than forty-eight hours.

C. *The Handling of the Developed Cases and the Prevention of Secondary Cases.*—As a general rule this problem is met by the transfer of all patients with the diagnosis of contagious disease to their homes or to a contagious disease hospital or unit, as dictated by the public health authorities, and the prevention of further admissions or discharges from all or part of the pediatric wards during the incubation period of that disease, with a similar procedure for all secondary cases.

Although such a plan does prevent the original case from causing any further contagion, it does very little to control secondary cases among the contacts. An even greater disadvantage (and this is particularly true in a teaching hospital) is the marked decrease in the number of hospital beds made available throughout the year, with a consequent decrease in the usefulness of the department. As a corollary of this decrease in patients, we have inferior teaching material. There results, furthermore, an economic loss to the hospital from unoccupied beds and a distinct hardship to the parents of those patients who, by reason of the quarantine, might be compelled to remain in the hospital well beyond their normal date of discharge.

It was just this problem which prompted Kereszturi, Hauptman, Park, and Bartlett to conduct a "no quarantine" experiment at the Fifth Avenue Hospital in New York City from 1931 to 1934. They paid special reference to two problems: one, the effect of omission of formal quarantine on the cross-infection rate, and two, the value of the various specific convalescent sera in preventing the development of the disease among contacts.

In their excellent review[1] these authors brought out the interesting fact that, although a great deal may be found in the literature concerning the virtues of various isolation methods in the prevention of cross-in-

fections in contagious hospitals, very little appears concerning the handling of the problem of controlling these diseases in the pediatric wards of general hospitals.

As the study by Kereszturi and associates is the only one of its kind[2] that we can find in the literature and because it prompted the modified plan which we have been following, a brief review of their plan and its results would seem necessary at this point.

After making every effort to prevent the admission of any patients with contagious diseases, they secured a complete contagious disease history from all patients admitted and did routine Schick and Dick tests. Immediately upon the development of any common contagious disease in the wards, that patient was removed from the hospital and all contact cases were then divided into three groups. Group I consisted of all children considered as immune to that disease, either because of age (under 6 months), a history of having had the disease, or, in the case of diphtheria or scarlet fever, a negative Schick or Dick test. The remaining or nonimmune children were then divided equally into Groups II and III, all children in Group II being given from 5 to 15 c.c. of the specific convalescent serum for that disease, or in the case of scarlet fever or diphtheria, specific antitoxin; while the remaining nonimmunized susceptible children constituted Group III.

In the course of their three-year study of 1,717 admissions, 29 children developed contagious diseases from which, in all, 37 secondary cases developed, a primary incidence rate of 1.7 per cent and a cross-infection rate of only 2.1 per cent of all admissions. This they compared with rates of 1.0 per cent and 2.2 per cent under the quarantine system during the two preceding years—showing little statistical effect from the abolition of quarantine. They found, however, that only in the instances of measles and mumps did the convalescent serum seem to lower the number of secondary cases, while in the chicken pox group more secondary cases developed among the immunized children than among the nonimmunized. In the instances of German measles, scarlet fever, and whooping cough no secondary cases occurred, while no primary or secondary cases of diphtheria developed. These findings prompted the authors to conclude that "the disadvantages of quarantine for a general pediatric service are much greater than the good achieved by its use."

Struck by the obvious value of such a plan, the Pediatric Department of the Hahnemann Medical College and Hospital of Philadelphia applied to the Department of Public Health of that city for permission to try a modification of this plan in their wards during 1938. After conferences with the late Dr. William C. Hunsicker, director of the department, and Dr. George E. Johnson, chief of the Division of Communicable Diseases, a plan was agreed upon and permission given to conduct the experiment.

III. OUTLINE OF THE PROPOSED SOLUTION AND APPRAISAL OF ITS RESULTS

By considering the three aspects of the problem as originally outlined, this plan can be summarized briefly as follows:

I. *Admission of Contagious Cases.*—The intern on pediatric service is required to examine all children in the examining room on the first floor of the hospital before they can be transferred to the pediatric wards. In case of any suspicion of any contagious disease, he is directed to obtain the confirmation of one of the more experienced members of the resident staff or of a member of the pediatric department and/or the district medical inspector of the Department of Public Health. He is further required to fill out, prior to transfer to the ward, a protocol giving a complete contagious disease history of the patient (Chart 1).

HAHNEMANN HOSPITAL-PROTOCOL FOR THE STUDY OF THE CONTROL OF CONTAGIOUS DISEASES

Name_____ Age_____ Date of Adm._____

Diagnosis_____ Result_____

History

(To be filled in by interne at time of admission. Give dates when possible)

DISEASE	WHEN IMMUNIZED	WHEN INFECTED	DATE OF EXPOSURE (RECENT)
Anterior Poliomyelitis			
Chicken Pox			
Diphtheria			
Rubella			
Measles			
Mumps			
Scarlet Fever			
Small Pox			
Whooping Cough			

Immunological Data

Schick Test_____ Dick Test_____ TBC Test_____ Wass. Test_____ Special_____

Immune Globulin Reactions: Local_____ General_____ Serum Adm. _____

Contagious Disease Data

Disease developed while in hospital_____ Disease developed in a contact during hospital stay_____ (Give name of disease, date of onset, nature of contact and severity)

Remarks:

This sheet is to be placed on the front of all charts for patients over one year of age admitted to the pediatric wards except tonsil cases, and must be filled in by the interne on the pediatric service.

Chart 1.—Protocol for study of the control of contagious diseases in the Pediatric Wards of the Hahnemann Hospital, Philadelphia, Pa.

II. *Admission of Cases During Incubation Period.*—Because everything pointed to an epidemic of measles in Philadelphia in 1938 and also because we wanted to study the relatively unsettled problems concerning the efficacy of and reactions from placental extracts, it was decided to give every child included in our study a 2 c.c. dose of immune globulin (human) intragluteally in the examining room. After this the child is transferred to one of two admission rooms on the pediatric floor (or in special instances to one of the four single bed isolation rooms) where he is kept for a minimum of forty-eight hours, with bed isolation technique. The constant turnover of cases rarely permits the continuation of this admission room isolation much beyond forty-eight hours. Infants under 1 year of age are not included in this study, not only because their age confers upon them a relative immunity to many of the contagious diseases, but also because they are housed in ward nurseries having no contact with the older children save through house or staff physicians. Children admitted for tonsillectomy and adenoidectomy are similarly removed from the general wards and consequently are not included.

III. *The Handling of Developed Cases and Contacts.*—All children with diagnoses of contagious disease are immediately sent either to their homes or the Philadelphia Hospital for Contagious Diseases at the direction of the District Medical Inspector from the Department of Public Health. As soon as possible after admission each child is given routine Schick and Dick tests, and in the case of all girls, a vaginal smear is made. Routine throat cultures for diphtheria bacilli were originally included in this plan, but the impracticability of having so large a number of smears examined regularly either by our laboratories or those of the city prompted the reduction of this procedure to suspicious cases only. Once a contagious disease developed in any of the rooms, all other children in that room not considered immune in the light of their past histories or skin tests are given second doses of from 2 to 4 c.c. of immune globulin (human) except in the instances of diphtheria or scarlet fever, in which case specific antitoxin is used.

Dick and Schick tests are done on all nurses, floor maids, and interns, and immunization is recommended for all found to be nonimmune. In those cases where immunization is not secured for any reason, such nonimmune persons are kept from the pediatric floor during the winter season. Discharge of patients sleeping in the same room with a contagious case is permitted only with the approval of the Department of Public Health, and the subsequent course at home of such patients is followed up carefully. Although no new admissions are made to the individual room from which the child with the contagious disease has been removed until all remaining children in that room have been discharged or the period of incubation for that disease has terminated, admissions to and discharges from the other rooms of the wards continue undisturbed.

An appraisal of the results of such a plan can best be made by comparing the number of admissions made possible under the plan with those possible when the former quarantine plan was in effect (the number of admissions being selected in preference to the total patient-days, since the latter figure might be influenced by patients kept in the wards by the quarantine); and by comparing the number of cases of the common contagious diseases developing primarily and secondarily under this plan with the number in the preceding years. It would also seem that some indication of the efficacy of the immune globulin (human) in the prevention of measles might be secured by comparing the case incidence for measles in the wards with that for the city at large, in this and preceding years.

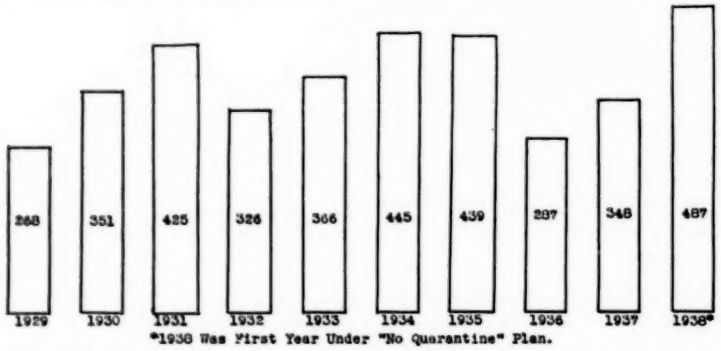

Chart 2.—Admissions to pediatric wards (excluding infants and patients admitted for tonsillectomy), Hahnemann Hospital, Philadelphia, Pa.

The influence of the plan upon the number of admissions is readily seen by reference to Chart 2. It will be noted that the total number of admissions (excluding infants under 1 year of age and children admitted solely for tonsillectomy and adenoidectomy) for the year of 1938 was 10 per cent greater than that for any of the preceding nine years, and 30 per cent greater than the average for this period. (It is probable that this figure should be even greater, for in the records of the earlier years of the decade tonsillectomy cases were not so readily separable from the others as in the past three years.)

As to the number of cases of contagious diseases, we note in Chart 3 that statistically there was little difference in the years included in this study. These figures would seem to show, however, that there was certainly no marked increase in secondary cases without formal quarantine. For 1938 the only secondary case was one of chicken pox in a student nurse exposed to a child admitted with a diagnosis of impetigo. It is interesting to note that of the six primary cases, two, one of scarlet fever and one of measles, were admitted on the same night, but fortunately to single isolation rooms. Upon diagnosis the following morning, they were

immediately transferred to the Philadelphia Hospital for Contagious Diseases, and, although admission and discharge continued unrestricted, no secondary cases developed. The single case of mumps was admitted under the diagnosis of cervical adenitis, one of whooping cough as bronchitis, and the fifth case, one of chicken pox, developed without known contact after the child had been in the hospital more than a month. The chicken pox case admitted as one of impetigo completes the list. In these instances the contact children in the same room who had not had the disease were given additional doses of immune globulin (human) and in none of these children did the disease develop.

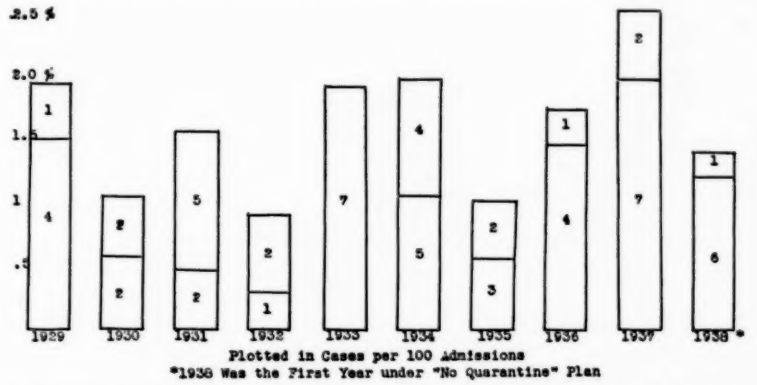

Chart 3.—Quarantinable cases in pediatric wards, Hahnemann Hospital, Philadelphia, Pa. Lower figures are for primary cases; upper, for secondary cases.

This gives a primary infection rate of 1.2 per cent and a secondary infection rate of 0.2 per cent. The relatively small number of cases makes these figures statistically unreliable, but the fact that no great increase in cases of contagious disease resulted under this plan is obvious.

The final point, that of a comparison between the case incidence of measles in our wards and among the children of the city as a whole, is illustrated in Chart 4. Data for the curve showing city-wide incidence was supplied by Dr. Joseph A. Scarano of the Department of Public Health. Here we note that the curves in general followed one another until 1938, when the case rate for the reported cases in the city at large was about 1.5 per 100 children and that for our group, about 0.2. Admittedly the number of cases is too small for any accurate conclusions to be drawn, but it can at least be noted that the case rate for 1938 in our wards was less than that for any preceding "measles year" in the last decade. A careful review of the 487 children who were given intragluteal injections of the immune globulin (human) reveals that in only one instance was there a moderate local reaction and in no case a general or systemic reaction.

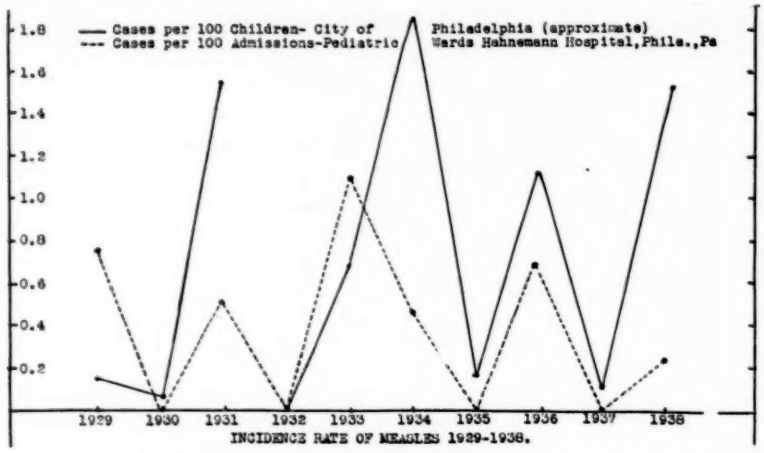

Chart 4.—Incidence rate of measles cases for children in city of Philadelphia compared with those admitted to the Pediatric Wards of the Hahnemann Hospital 1929-1938.

SUMMARY AND CONCLUSIONS

The obvious disadvantages of the customary methods of handling contagious diseases in the pediatric wards of general hospitals by formal quarantine of all or part of the wards justify further trial of such plans as that employed at the Fifth Avenue Hospital in New York City. A modification of this plan was tried in 1938 at the Hahnemann Hospital in Philadelphia.

By this plan an increase of 10 per cent over the highest number of admissions for any preceding year in the decade was achieved with an average increase of 30 per cent for that period.

No increase in the number of primary contagious diseases developing under this plan took place, while the number of secondary cases was as low as that for any preceding year.

In spite of a widespread epidemic of measles throughout the city the only case encountered among the 487 admissions was admitted in its full-blown state. The routine use of immune globulin (human) as a preventive seems worthy of continued trial.

Of the 487 patients given routine intragluteal injections of the immune globulin (human) only one showed a moderate local reaction and none showed any general or systemic reaction.

Further development of such plans for the control of contagious diseases in the pediatric wards of general hospitals seems indicated.

Note.—Since this article was written there has appeared an article, "The Prophylactic Use of Parental Blood Serum Against Contagion in a Pediatric Ward," by Barenberg, Greene, and Grand,[2] from the Pediatric Service of the Morrisania City

Hospital, New York, N. Y. These authors also stress the disadvantages of the quarantine system and further discuss the inadequacy of proper isolation in a general hospital. To meet this problem they have injected 20 to 30 c.c. of parental blood serum intramuscularly into every patient admitted into the pediatric medical wards. By this method they have been able to maintain a constantly open ward free from outbreaks of contagious diseases. Of a total of 2,095 susceptible patients admitted during the period covered by this study, 10 cases of primary contagious diseases developed, a case incidence rate of only 0.5 per cent. No secondary cases were reported.

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MULTIPLE CYSTIC TUBERCULOSIS OF THE BONES

Report of a Case

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APPARENTLY this is the twelfth case of multiple cystic tuberculosis of the bones to be reported in pediatric literature.[1]

CASE REPORT

A. W. (No. A 12493), a 6-year-old colored boy, was admitted to the Duke Hospital Dec. 12, 1938, complaining of swelling of the left elbow for nine months and swelling of the left foot for seven months.

Family history was negative except for the fact that the patient was exposed to tuberculosis at the age of 3 years while living with an aunt who died of the disease.

Past history was negative also, except for pertussis at the age of 1 year and a poor diet.

Present Illness.—In March, 1938, nine months prior to his admission to the Duke Hospital, a painless swelling developed at the left elbow. No redness, increased local heat, or limitation of movement was noted; however, the joint increased gradually in size for the next four or five months and then remained stationary. The elbow was painful only on forcible pressure. At the onset the patient also complained of pain in the epigastrium and right costal margin. The aching pain was occasionally associated with nausea and vomiting, but it had no relation to meals or respiration. The pain continued intermittently until four months prior to admission. In May, 1938, seven months prior to his admission, a similar painless swelling appeared at the dorsum of the left foot, and increased slowly. During the entire illness the child had marked anorexia and lost considerable weight. There was no history of cough, sputum, night sweats, or hemoptysis.

Physical Examination.—Temperature was 39° C. (102.2° F.); pulse rate 124; and respiration rate, 26. The patient was emaciated (Fig. 1). His skin was loose and dry with dark pigmented scales over both lower legs. The anterior cervical, axillary, right epitrochlear, and inguinal nodes were palpable, but not enlarged or tender. The tonsils were hypertrophied and appeared chronically infected. The percussion note over the right upper chest posteriorly was slightly impaired, and there were some suppression of the breath sounds and occasional fine râles. The abdomen was scaphoid, and the liver and spleen were not palpable. The left elbow was markedly deformed with a fusiform distention of the joint capsule. The swelling of the elbow was fluctuant with slight increase in local heat but no erythema, pain or limitation of motion (Fig. 2). The right elbow and dorsum of the left foot also had slight fusiform swellings. The remainder of the joints appeared normal.

Accessory Clinical Data.—The hemoglobin content was 7.5 gm. (50 per cent Sahli); red blood cell count, 2,700,000 with central achromia; white blood cell count 10,250 with 78 per cent polymorphonuclear cells, 18 per cent small lymphocytes, and 4 per cent monocytes; urinalysis showed a specific gravity of 1.028 with

From the Department of Pediatrics of Duke University School of Medicine and Duke Hospital.

2 to 3 white blood cells per high-power field; sugar, albumin, and Bence-Jones test for protein were negative. Tubercle bacilli were found in the gastric washings; intradermal tuberculin test (1:1000) was ++; Wassermann reaction was negative; serum calcium, 8.8 mg. per cent; and plasma phosphorus 5.4 mg. per cent.

Fig. 1.—Photograph showing emaciation of the patient and increase in the size of the left elbow.

X-ray examination of the chest showed advanced childhood tuberculosis with thickened pleura over the right chest. Films of the left elbow showed a diffuse periostitis involving the adjacent ends of the humerus and ulna with marked soft tissue swelling (Fig. 3). The right elbow had a localized area of bone destruction without any attempt at regeneration in the medial humeral condyle in which there were three large punched out areas (Fig. 4). Roentgenograms of the spine, knees, feet, ribs, clavicles, scapulae, pelvis, and lower extremities were entirely negative.

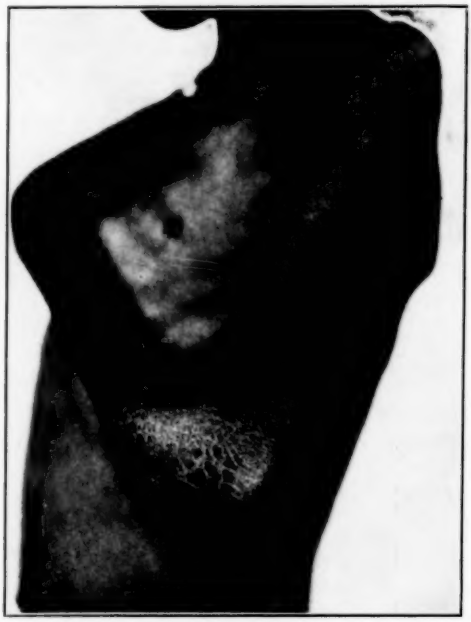

Fig. 2.—Photograph showing fusiform swelling of the left elbow with limitation of the deformity to the joint capsule.

Fig. 3. Fig. 4.

Fig. 3.—X-ray film of the left elbow showing marked periosititis of the humerus and ulna.

Fig. 4.—X-ray film of the right elbow showing typical punched-out areas of bone destruction in the medial humeral condyle.

DISCUSSION

The eleven cases of cystic tuberculosis of bones reviewed by Law and Perham[1] were characterized by swelling of the parts involved, which usually was painless, a positive tuberculin test, and evidence of intrathoracic tuberculosis. The bone lesions were most commonly found in the smaller bones of the extremities; however, they were also demonstrated in the humerus in three of the ten cases. Roentgenograms showed cystic destructive processes in the bones, and in the case reported by Law and Perham the periosteum of the shaft of the humerus was elevated. The osseus lesions gradually improved. Our case is similar to the others, except for the marked periostitis of the left humerus.

Hyperparathyroidism and multiple myeloma were ruled out by the absence of a generalized decalcification, the normal serum calcium and plasma phosphorus, and the absence of Bence-Jones protein reaction in the urine. Boeck's sarcoid seems unlikely. Law and Perham's suggested explanation for the rarity of this lesion seems logical, i.e., after an infection of the blood stream, the tubercle bacillus localizes in the metaphyses of the bones because of the anatomic situation of the end arteries; the caseous process of a tuberculous lesion of a bone usually is more rapid than fibrosis and may lead to abscess or sinus formation; and generalized tuberculous infections in children are likely to end in death in a relatively short time.

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Special Article

ADOPTIONS

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ADOPTION is an old and well-recognized procedure whereby an individual or family assumes the responsibility of rearing a child of whom they are not the natural parents. Only within recent years has society recognized that the process of adoption has well-defined social, legal, and medical implications which require the careful consideration and the mature judgment of all the parties involved and often the advice and counsel of trained workers.

The mere recognition of the complexity of the adoption problem has not resulted in the taking of the steps necessary in order that those concerned will be protected from future disappointments. One might add that, even in those states where adoption laws have been enacted, many individuals are evading and avoiding the very protection to which the law entitles them. The feeling prevails that legal proceedings are in many instances long drawn out, cumbersome, confusing, and altogether too technical for the layman's understanding.

Notwithstanding the fact that the first adoption laws in the United States date back to 1851, there remain 22 states which permit of the transfer of guardianship or giving up the custody of children without court action or without the approval of any recognized welfare agency. Such records as are available seem to indicate that the number of children adopted in this informal way, that is, without a thorough investigation relating to family background, the essential health examinations and psychological tests for the adoptive child, and without any consideration being given to a probationary period, outnumber all adoptions which are safeguarded in part at least by certain legal protection.

Society has, however, gone a long way in assuming its responsibility toward the child since the days when their very existence depended upon the whims of the parent or the need of the state—that dark era when the child was sacrificed on the altar of ignorance, greed, and superstition.

Adoptions as carried out at the present time under the most satisfactory conditions are the result of the decades through which civilization has made slow and interrupted headway and bear witness to the fact that the child has played an important part in these advances. Society's

One of a series of articles prepared for, approved by, the Committee on Mental Hygiene, American Academy of Pediatrics.

attitude toward the child and his rights may well be taken as a criterion of the state of civilization which any given community has reached.

Ill-advised, speculative transactions in human relations can only end in disaster. An adoption should be considered as an investment in all the finer feelings that should be built up within a family circle, those feelings which give all concerned a sense of worthwhileness and security.

Although there are no statistics to guide us as to the relative merits of the casual, indifferent, haphazard way in which most adoptions are carried out as compared with an intelligent, well-organized plan involving a careful medical and social scrutiny of the entire situation, it is reasonable to suppose that the latter plan will pay better dividends, that knowledge of any problem is likely to prove useful in making important decisions and that the understanding of the varied factors as well as the individuals involved in the adoption situation should constitute one of the important elements leading to a successful adoption.

We must keep in mind that every adoption represents a great adventure in the adjustment of human relationships. Its implications are tremendous; its effects are profound. Success brings joy, failure unmitigated sorrow. Therefore, society should not be tolerant or satisfied to allow conditions to exist which are the result of indifference and which lead to and encourage speculative transactions in children and permit their future happiness to become a mere matter of chance.

The great majority of homeless, unwanted children are shifted about from agency to agency, from institution to foster home and back, finally landing by mere chance in an environment that is good or indifferent or, what is far more frequent, positively bad, and without any of the essentials upon which to build a sense of security for either the present or the future.

The present standards being advocated and practiced by certain private adopting agencies appear to be such that only a relatively few presumably exceptional children will be placed with foster parents and in homes that are definitely better than average from the social and economic point of view, and with foster parents who as individuals are free from the common instabilities, defects, and frailties with which the average mature individual is usually afflicted. I dare say that if the children of natural parents were subjected to the same intensive, scrutinizing investigation from the doctor, social worker, psychologist, and other specialists who are brought in to pass upon the prospective adoptive child, a relatively small per cent would be looked upon as being acceptable by such an examining body and, like the undesirable offspring of the Spartans, they would succumb to the rigors of the elements.

Notwithstanding that important advances have been made during the past twenty years relating to the responsibility of the state in safeguarding the interests of the child, the natural parents, and the adoptive parents, and the wise legislation that has been enacted in many states

requiring investigation of the adoptive child and the adoptive parents (and the fitness of both, in order that reasonable chances for success will ensue from the procedure of adoption); the fact remains that relatively few of the prospective adoptive children are benefiting by the modern contributions of medicine, psychiatry, psychology, and social work, and that a very large percentage of all children being placed in adoptive homes without adequate investigation and a similar number of adoptive parents are taking unnecessary chances and receiving none of the protection to which they are entitled.

The solution to the problem is by no means simple. There are certain definite concepts in relation to adoptive procedures which should be accepted:

That every parentless child is entitled to adequate care and protection and a substitute home which, so far as possible, approaches what might have been a normal home.

A recognition of the fact that there are certain children who, by virtue of mental defect, physical handicaps, and an hereditary background of such a nature that would be likely to jeopardize the child's future development, are not looked upon as being good risks, even for adoptive parents willing to assume the ordinary responsibilities and obligations of rearing children.

There are individuals who, by nature of mental defect, mental disease, emotional instabilities, defective moral standards, financial limitations, and who because of incompatibilities arising from matrimony itself, are not suitable to assume the responsibility of rearing children.

It is fair to assume that there is a large number of what may be termed adoptable children, from the definition just given, and a large number of childless parents, relatives, stepparents, and others, who, for good and sufficient reasons, desire to assume the legal responsibility of rearing one or more children not their own, who should be brought together.

The problem at the moment is not one of getting the perfect child into the perfect home, but rather the broad, sociologic problem of bringing together the largest number of acceptable children and the largest number of acceptable homes, with the objective of increasing the sum total of the satisfactions to be derived by both adoptive parent and child, and with the minimum amount of risk of creating incompatible relationships.

Such a plan cannot be effectively put into operation unless careful, painstaking investigations be carried out by a well-trained group of specialists who, by virtue of their investigations, will determine all of the obvious reasons why an adoptive procedure would not be successful and many of the reasons that would not be recognized by untrained workers. They would be in a position to recognize, understand evaluate, and interpret what might well be called reasonable liabilities which must be

assumed by both adoptive parents and adoptive child, comparable to the liabilities that invariably occur in the natural parent-child relationship.

The plan as outlined cannot be effectively carried out if standards are set so high for an acceptable adoptive home and what may be termed an acceptably adoptable child that the relationship must be theoretically free from all of the pitfalls that normally exist in the parent-child relationship.

Although it is reasonable to expect that the elimination of what may be termed reasonable liabilities which both parent and child should assume through the adoptive procedure would result in a larger percentage of satisfactory placements, however, by setting standards too high, we immediately eliminate all possibility of placing a large number of desirable children in desirable homes which we have reason to believe will eventually work out to the advantage of both child and parent as well as society.

We are not unmindful of the fact that even when adoptive procedures are carried out on the high level of efficiency as is set up by the accepted private adopting agencies, mistakes sometimes of a serious nature are made. Some important step in the family investigation is overlooked; deceits have been practiced by parties involved; and investigations failed to reveal important facts; furthermore, we recognize that all medical and psychologic tests are not infallible. This in no way casts any reflection upon method or effort. We are also cognizant of the fact that adoptions which have been carried out in a haphazard, speculative sort of way have turned out successfully. Here, again, one is not putting approval on such methods.

The all-important and practical point to be considered is that, so far as possible, the maximum number of adoptive children and acceptable adoptive parents and homes should benefit by such scientific procedures as are available at the present time, in order that all reasonable safeguards should be given to all concerned.

The problems of the adopted child are those that occur in the process of growing up and are not necessarily different from those of the child being reared by natural parents. There are, however, certain situations to which the adoptive parent has to make adjustments that are not common to the natural parent-child relationship; and as one reviews the development of the problems related to adopted children, it becomes quite obvious that certain emotional responses on the part of the adoptive parents do play an important part in perpetuating if not creating the problem. Often the adoptive parent, especially the mother, embarks upon her job with a deep-seated conviction that she has a mission in life to perform, and not infrequently the intensity, fervor, and passion with which she endeavors to fulfill all of her obligations and responsibilities as a mother are quite overwhelming to the child and result in an over-

solicitous, unduly affectionate and protective attitude on the part of the parent, and often result in creating a dependent, egotistical, demanding, undisciplined child whose conduct is but little influenced by praise, blame, rewards, or punishment. Such a child is obviously selfish and unmindful of the welfare of others. This oversolicitous type of individual, whether it be a natural or an adoptive parent, would be likely to create the same attitudes in the child.

The adoptive mother who is invariably from six to ten years older than the natural mother and who has spent these years anticipating the joys and satisfactions of parenthood, is now doomed to disappointment. In return for all of her sacrifices, her zeal, and wholehearted devotion, she finds herself embroiled in a relationship out of which she is getting little satisfaction. In her efforts to explain the undesirable personality traits which have developed in the child notwithstanding her interest and solicitude, she seeks the answer in terms of inheritance. In spite of how much or how little the adoptive parent may know of the child's background, when one begins to develop doubts and misgivings as to the fundamental structure of the material with which he has to work, the confidence and sense of security which are obsolutely essential in order to do a constructive job in child training are shattered.

Many of the ordinary everyday situations that occur in the life of the average child become endowed with an importance of a queer mysterious nature when parents get entangled and baffled with the problem of inheritance.

Another situation that not infrequently creates problems with reference to adoptions is that the idea of adopting the child is not always acceptable to both parents. It may be said that the procedure is usually initiated by the wife and that husbands as a rule simply trail along, oftentimes reluctantly. It appears that children satisfy quite different emotional urges or needs in the woman than they do in the man. With a prospective adoptive mother the motivating force is undoubtedly that of the so-called "maternal instinct"—the desire to nurture, protect, love, serve, to be needed, wanted and indispensable to the life of the child. All these drives are satisfied undoubtedly in most cases to a greater degree than are the egoistic drives of the male which are related to the desire on the part of the man for self-perpetuation, the development of the idea that the offspring is part of himself whose very existence is dependent upon the father. These ego drives are more self-centered and less well endowed with the finer emotions which characterize the maternal instinct.

This does not mean, however, that the adoptive father does not build up a satisfactory emotional relationship with the adoptive child, for as the relationship develops, the importance of the more primitive selfish ego strivings become lost or become less marked. One learns from ex-

perience that one does not love individuals because of certain relationships whether it be father, mother or child—one loves them because of certain qualities that are compatible between individuals which permit a satisfactory relationship to develop.

There is nothing fundamental in the adoption procedure which should prevent such a relationship. It is oftentimes important, however, for prospective adoptive fathers to understand the emotional implications that occur during the early considerations of adoptions and what they have a right to expect from the relationship as time goes on. This, of course, does not mean that an adoption should be carried out against the wishes of either the prospective adoptive mother or father. It simply indicates that it is but natural that the adoptive mother embarks upon the procedure with more enthusiasm.

Much has been written with reference to the part which the motives of the prospective adoptive parents play in the success of adoptions. These motives are numerous and varied. Not infrequently the adoption procedure is used as an effort to patch up a bad marital situation. Less frequently the adoptive parents are thinking in terms of economic support or some additional comfort during their advancing years, or perhaps some other outstandingly selfish desire. Now and again we find that pity for the parentless child or a sense of obligation to a member of the family or friend exerts such a strong temporary emotional influence as to initiate adoption procedures which are regretted later. By far the most common and far-reaching motive, however, for adoptions is that urge emanating from childless couples who feel the need of having a child in the home in order that their happiness may be more completely fulfilled and in order to round out a better type of social existence and to more adequately meet what they feel to be the real purpose of their existence. With this latter group the altruistic and selfish motives are bound to get somewhat entangled one with the other, but on the whole, as a group, they may be considered good and adequate reasons for wanting to adopt a child and if such motivating forces are not adequate and do not lead to successful adoptions the whole adoption procedure must be looked upon as a failure, for obviously much of all the adopting that has gone on in the past and will continue to go on in the future will be done by those who do not have children of their own and for some reason or other feel the need of enlarging the family circle.

Ordinarily prospective adoptive parents are not deceived in their reasons for seeking to adopt a child. They do, however, frequently allow themselves to be deceived with reference to the responsibilities and the obligations which the process involves and perhaps in a sort of idealistic way exaggerate the satisfactions and compensations to be derived from the anticipated steps. These same responsibilities and disappointments are not infrequently in store for the so-called "normal parent."

The medical aspects of an adoption situation are well understood by the average physician. He is quite aware that the parental background of every child should be carefully investigated for the purpose of determining whether or not there exists a history of hereditary defects of such a nature that well might jeopardize the future development of the child. When there is a background of mental disease, mental deficiency or epilepsy, or other abnormalities of a psychopathic nature the physician must attempt to determine just how important these hereditary defects may be in the life of this particular child. Another question arises as to the importance of such aspects of the family history which cannot be obtained. Inasmuch as adoptions are frequently associated with illegitimacy, the absence of any history of the parental background complicates the situation. Here again consultation with a social agency is frequently the solution. A painstaking physical examination with such laboratory tests as would establish the physical fitness of the child should, of course, be a routine of every adoption. Tuberculosis, syphilis, hemophilia, and other physical familial defects should be eliminated.

As already stated, the interpretation of what is disclosed in these examinations is often most difficult and must necessarily reflect the skill and experience and perhaps the philosophy of the particular individual doing his particular part of the job. There are very important reasons why all the available information: medical, social and psychologic, should be gathered together and evaluated in terms of the family background, the history of the physical growth and mental development of the child, and the intellectual background and the emotional stability of the adoptive parents. In brief, the whole child must be evaluated in the most objective physical and psychologic terms; the prospective parents should be subjected to similar tests, and the new environment adequately evaluated from a sociologic point of view. It is, therefore, reasonable to expect a well-organized agency, staffed by those trained and experienced in the use of tools and methods for carrying out a sociologic investigation, familiar with, and capable of utilizing, all the available facilities which the community provides, is in a position to render valuable service to the natural parents, adoptive parents and, what is most important, the child. Such service should give to all concerned the best possible chance for success in carrying out the adoptive procedure by eliminating so far as possible the ordinary pitfalls upon which many adoptions become wrecked. The problem, as it concerns society at the moment, is to bring the maximum number of average children and average homes in contact with one another, assuming what may be considered to be the average risk of failure and disappointments that would be likely to occur in building up such a relationship.

Frankness is absolutely essential in carrying out the adoption procedure. There is no room for secrecy or misinformation either in regard

to the information which the doctor or agency should give the adoptive parents or in the relationship between the adoptive parents and the child. Normal parents enjoy the right to, and profit from, the knowledge which may be derived from familiarity with the family background, and there seems to be no reason why adoptive parents should not profit from having all knowledge that is available with reference to the child for whom they are responsible. Ignorance is no protection against disaster either for the child or for the parents.

Hereditary factors, either good or bad, should neither be featured nor ignored, and the adopted child should be told frankly and honestly and without too much sentimentality about his adoption. It is the only safe way in which a happy relationship between adoptive parents and child can be built up. This relationship, like that existing between parent and child in general, must necessarily weather some stormy periods and occasionally a few gales. However, deception is never a safe retreat in time of storm.

The physician is in a position to advise the prospective adoptive parents as to the wisdom of embarking upon this important venture. He is ordinarily familiar with the family background, the reason for wanting the adoption, and just what the adoption may mean to both the parents and the child in way of happiness. The physician is also in a position to guide and direct the parents in the selection of a suitable child and contribute much that is of value in helping them interpret the hereditary background and the medical findings.

It may be said, however, that whenever the services of an agency can be utilized, which is equipped to approach the problem of adoptions from all of its varied angles, medical, social, psychological and legal, the physician will do well to allow these professionally trained people to do the job, the doctor acting in the capacity of the family adviser and cooperating with the agency and family to bring about a satisfactory result.

There should be a greater number of well-supervised adoptions which can only be brought about by a cooperative effort on the part of the families involved, the physician, and the adopting agencies.

Graphic Review

MORTALITY AMONG INFANTS AND CHILDREN AND PROGRESS IN REDUCTION OF RATES FROM CERTAIN CAUSES

HAROLD C. STUART, M.D.
BOSTON, MASS.

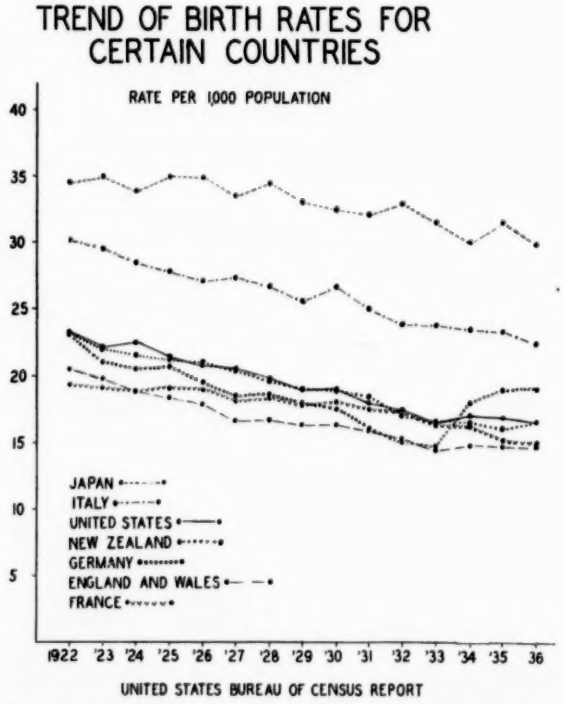
IN PREVIOUS reviews[1] the changing picture of child health in this country has been described, and tables have been presented which indicated the trends of certain mortality rates for preceding years. In this review Table I* shows the trends of these rates during the five-year period 1933-1938. It is an abbreviated form of a table appearing in a recent issue of Public Health Reports.[2] It shows gratifying progress in both infant and maternal mortality, as well as in the specific rates for the diseases listed. Although most of the latter are not based upon the child population alone, they reflect directly, and often primarily, conditions obtaining among children.

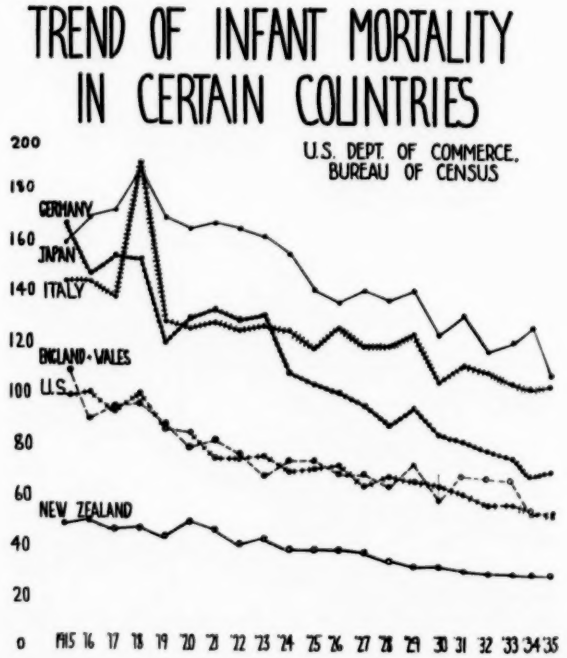
The description of conditions, as reflected in mortality statistics, is being omitted this year and a graphic portrayal is being substituted. For many of us, numerical tables and discussions of rates are dull and difficult to appreciate. Diagrammatic representations of such statistical material frequently tell the important facts briefly and leave a more lasting memory. It is felt, furthermore, that many pediatricians would appreciate having ready at hand an assortment of charts which collectively suggest the progress that has been made in saving the lives of children and indicate the major problems which remain to be dealt with. It has not been possible to deal with all aspects of child health in this way, but the charts which follow show the trends for a variety of conditions.

The latest Mortality Report of the Bureau of the Census is for the year 1936, but in a few instances later provisional figures are available. Most of the charts presented have been revised on the basis of the 1936 figures. Occasional charts representing local areas have been used primarily because of availability, but they have been considered representative of more general conditions in comparable areas.

The charts which follow may be studied with profit from various points of view. One may consider the factors that have been accountable for the changes in specific rates. One may speculate as to why some rates have fallen, while others have shown little change, why some rates are so different in different communities, and to what extent the unfavorable rates are beyond present control. The answers to these questions cannot be given in positive terms, but a thoughtful consideration of the issues raised may call attention to the inadequacies of current preventive procedures. The legends to the individual charts are not intended to constitute thorough analyses of the data which they contain, but merely to orient the reader in his study of them.

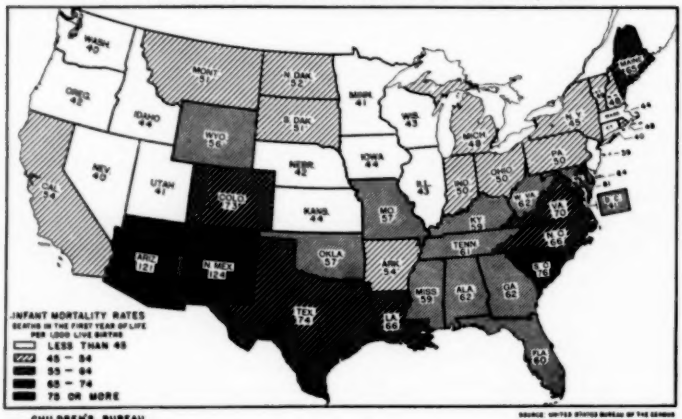
*Table I appears at end of article.





Charts 1 and 2.—In comparing the curves for the countries presented in these charts, it will be noted that Japan and Italy have both the highest birth rates and the highest infant mortality rates. The birth rates for the other countries have continued much alike and have shown a constant decline, except that in Germany the curve has been reversed since 1933. Germany has made the most striking progress in the proportionate reduction of the infant mortality rate since 1915, while New Zealand maintains the best ratio between births and infant deaths.

INFANT MORTALITY IN THE UNITED STATES, 1937



CHILDREN'S BUREAU
UNITED STATES DEPARTMENT OF LABOR

(7937)

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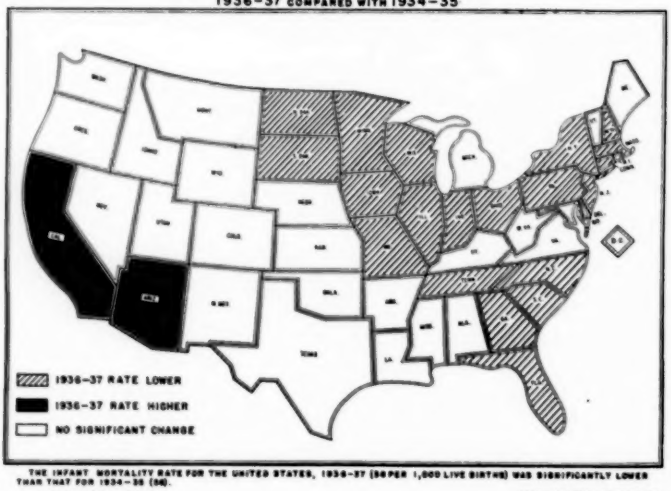
CHANGE IN
INFANT MORTALITY RATES
1936–37 COMPARED WITH 1934–35



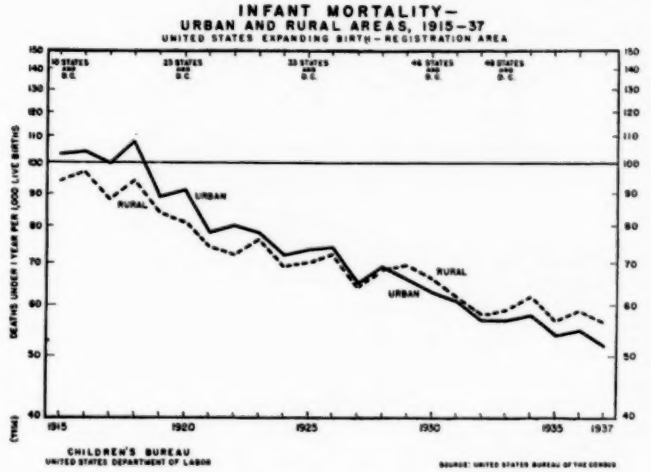
THE INFANT MORTALITY RATE FOR THE UNITED STATES, 1936–37 (50 PER 1,000 LIVE BIRTHS) WAS SIGNIFICANTLY LOWER THAN THAT FOR 1934–35 (56).

CHILDREN'S BUREAU
UNITED STATES DEPARTMENT OF LABOR

COMPILED FROM REPORTS OF
U.S. BUREAU OF THE CENSUS

Chart 3.—The differences in conditions throughout the United States are strikingly portrayed here. Although there are obvious reasons for higher rates in some areas than in others, as for example, a large colored population and a low economic status in certain southern states, there are undoubtedly conditions existing in some of the high rate states which could be corrected. It should be possible at least to cause the rates in the less satisfactory areas to approach toward those found in the more satisfactory regions.

Chart 4.—The regional grouping of the states in the different categories distinguished by this chart is very striking. The higher rates in California and Arizona may be attributed in part at least to the large influx of a poor migratory population, living under conditions which make the control of infections and nutritional disturbances difficult. Otherwise, the country is nearly divided into two parts on the basis of improvement as against no significant change within the period covered.



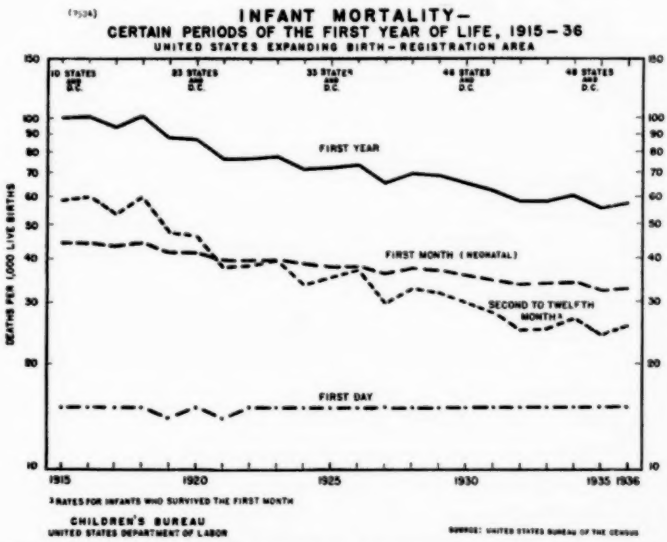


Chart 5.—Since 1928 mortality rates have favored urban rather than rural life for infants for the first time in the United States. A more rapid decline in urban than in rural birth rates may explain this change in part, but the more intensive efforts to protect infant health on the part of urban communities and the greater accessibility of health services in these communities has undoubtedly been an important factor.

Chart 6.—The differences in the rates of decline in mortality during the succeeding periods of the first year are well recognized, and the lack of improvement in the neonatal rates has been widely publicized. This chart shows that there has been a definite and steady decline in the neonatal curve during these years, and it appears insignificant only in contrast with the remarkable decline in the rates for the remainder of the first year.

Chart 7.—The groups of causes of infant deaths have varied in their contributions to the decline in the total infant mortality. This analysis of the decline by principal causes has been based upon figures for Massachusetts but is representative of occurrences elsewhere. The diseases of the digestive system, including diarrhea and enteritis, have contributed most, and the congenital and natal causes least, to the total decline, but progress with the latter group has not been inconsiderable. The congenital and natal causes account for approximately half of all infant deaths at the present time.

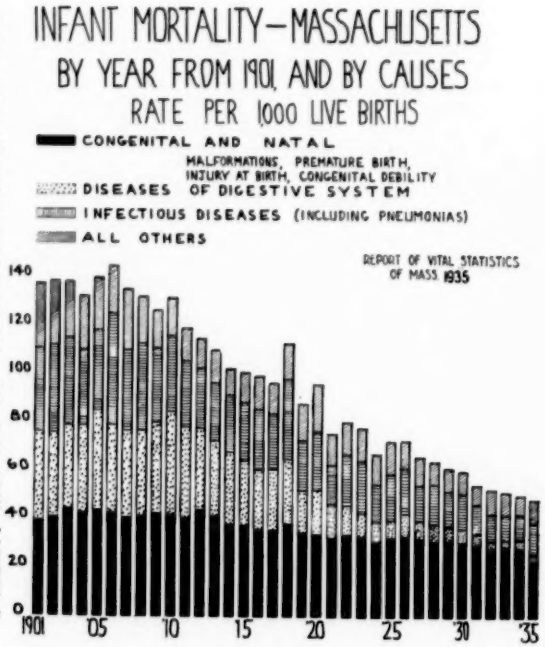
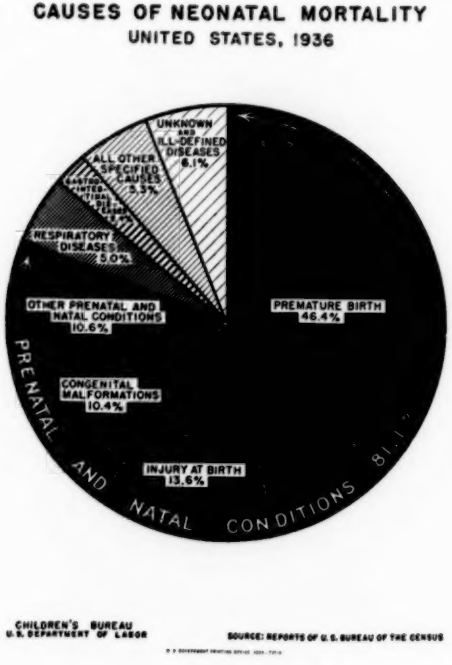


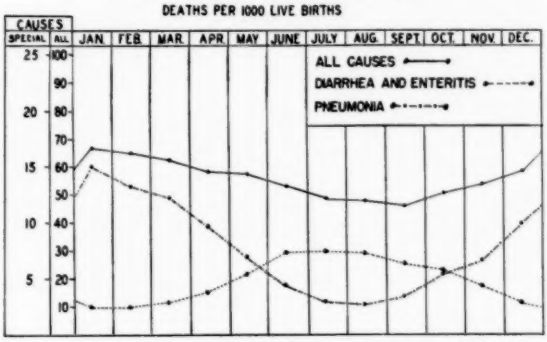
Chart 8.—The causes contributing to the high neonatal mortality which has been so resistant to change are here shown in their relative importance. The causes shown in black in Chart 7 are also represented in black here. The importance of premature birth as a cause of neonatal mortality is overemphasized in this chart, for it is often only a contributing cause, the death really belonging in one of the other groupings.


CAUSES OF NEONATAL MORTALITY
UNITED STATES, 1936
UNKNOWN AND ILL-DEFINED DISEASES 6.1%
ALL OTHER SPECIFIED CAUSES 5.3%
RESPIRATORY DISEASES 5.0%
OTHER PRENATAL AND NATAL CONDITIONS 10.6%
PREMATURE BIRTH 46.4%
CONGENITAL MALFORMATIONS 10.4%
INJURY AT BIRTH 13.6%
PRENATAL AND NATAL CONDITIONS 81.1%
CHILDREN'S BUREAU
U.S. DEPARTMENT OF LABOR
SOURCE: REPORTS OF U.S. BUREAU OF THE CENSUS

SEASONAL VARIATIONS IN INFANT MORTALITY

UNITED STATES BIRTH REGISTRATION AREA-1935

DEATHS PER 1000 LIVE BIRTHS



DEATHS FROM DIARRHEA IN INFANCY BY MONTHS

MASSACHUSETTS

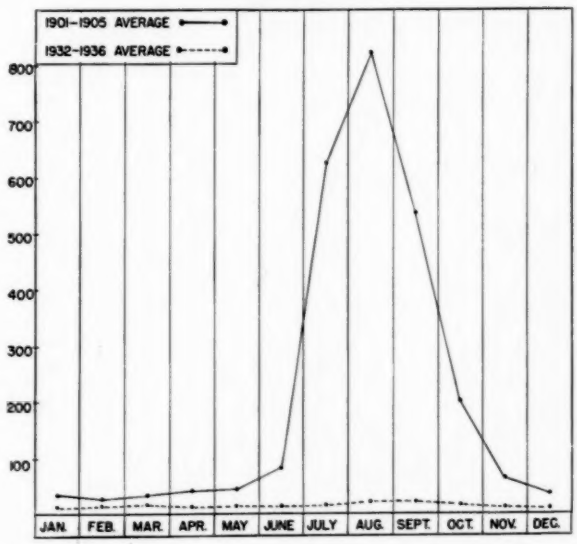


Chart 9.—With the reduction that has taken place in the number of deaths due to summer diarrhea and the less satisfactory progress in the prevention and treatment of respiratory infections, winter has become the most hazardous season for infants.

Chart 10.—This chart portrays one of the most notable achievements of preventive medicine and public health. Season is no longer an appreciable factor in determining the mortality from diarrhea in infancy in Massachusetts, although the preceding chart shows that it still is important for the country as a whole.

Chart 11.—The leading causes or groups of causes of death at each age are shown in the order of their importance and in respect to the total number of deaths for which they are responsible. The prominence of preventable diseases such as syphilis and diphtheria at certain ages constitutes a challenge. The relative safety of the fifth year of life is to be noted, no single disease except diphtheria causing 400 deaths among 5-year olds in 1934. The chart has not been revised for 1936 because the relative picture has remained much the same.

Chart 12.—The same arrangement of leading causes of death has been followed as in Chart 11, but the congenital and natal causes have been excluded from the "Under 5 years." column. The 10 to 14 year age period is seen to have the fewest causes of frequent deaths. The shift in relative importance of different causes at succeeding periods is of interest, especially the increasing prominence of tuberculosis and automobile accidents. It is startling to note that, although pregnancy and childbirth can only affect half the population, this group of causes ranks sixth among 15- to 19-year-olds, and fourth in the next age bracket. The high position of homicide and suicide among children 15 to 19 is also surprising.

LEADING CAUSES of DEATH by AGE U.S.B.R.A. 1934 BIRTH-5 YRS.

Deaths Per Yr.	UNDER 1 YR. 130,185	1-2 20,447	2-3 10,208	3-4 7,069	4-5 5,451
35,102	Premature Birth				
18,685	The Pneumonias*				
15,000	Diarrhea + Dysentery				
10,000	Congenital Malformations				
9,860	Injury at BirTh				
5,000	Congen. Debility	The Pneumonias*			
2,000	Influenza* Whooping Cough*	Diarrhea + Dysentery			
2,000	Suffocation * Thymus	Measles	The Pneumonias*		
1,000	Syphilis Measles Upper Respiratory	Whooping Cough* Influenza*	Diarrhea + Dysentery	The Pneumonias*	
1,000	Infest. Obst. + Hernia	Tuberculosis	Measles		
500	Meningitis* Tuberculosis Convulsions Erysipelas	Diphtheria	Diphtheria Influenza*	Diphtheria	The Pneumonias*
500		Upper Respiratory		Diarrhea + Dysentery	
400		Burns	Whooping Cough* Tuberculosis	Measles	Diphtheria

*Average over Five-year Period 1930-1934
(Tuberculosis Influenza, Meningitis - Include All Forms)

LEADING CAUSES OF DEATH BY AGE PERIODS U.S.B.R.A. 1934

Deaths in Given Age Period	UNDER 5 YRS 173,360	5-9 INC. 20,041	10-14 17,062	15-19 26,885	20-24 37,099
	(Excluding Congenital + Natal Causes)				
27,133	The Pneumonias*				
20,563	Diarrhea + Dysentery				
8,000	Influenza*				Tuberculosis
5,000	Whooping Cough*				
5,000	Measles			Tuberculosis	Auto Accidents
2,000	Tuberculosis Diphtheria	The Pneumonias*		Auto Accidents The Pneumonias*	Suicide + Homicide Pregn. + Childbirth The Pneumonias* Heart Disease
2,000	Syphilis	Auto Accidents	Appendicitis	Appendicitis	Appendicitis
1,000	Upper Resp. Meningitis* Burns Infest. Obst. + Hernia Suffoc + Thymus Auto Accidents	Appendicitis Upper Resp. Diphtheria	The Pneumonias* Auto Accidents Tuberculosis	Heart Disease Pregn. + Childbirth Homicide + Suicide	
1,000	Scarlet Fever	Measles	Drowning	Drowning	
500	Appendicitis Malaria Convulsions	Heart Disease Tuberculosis Scarlet Fever Meningitis		Upper Resp.	Upper Resp.

*Average over Five-year Period 1930-1934
(Tuberculosis, Influenza, Meningitis - Include all Forms)
(Heart Disease includes Pericarditis, Acute Endocarditis, Chronic Endocarditis, D's of the Myocardium, D's of the Coronary Arteries + Angina Pectoris and other D's of the Heart)

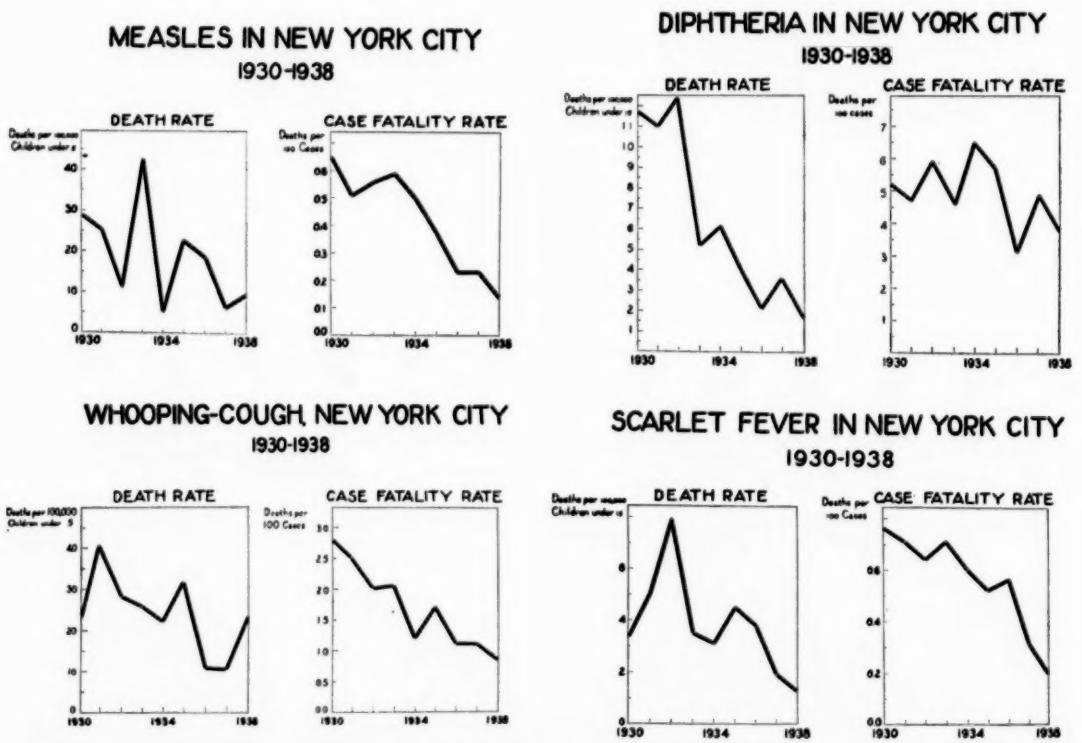


Chart 13.—Undoubtedly many factors have been operative in producing the decline in the rates shown in these graphs. The sharp decline in the death rate for diphtheria can be attributed in large part to the widespread application of immunization procedures. The explanation of the declines in the other death rates is more difficult.

The gratifying decline in the fatality rates can hardly be attributed in full to a sudden falling off in the reporting of cases or to a diminishing virulence of the infective agents. The results may be considered due in some measure at least to the prevention of infection during the early years when fatality rates are high, to better health among the children acquiring the disease, and to improved facilities for their care and treatment.

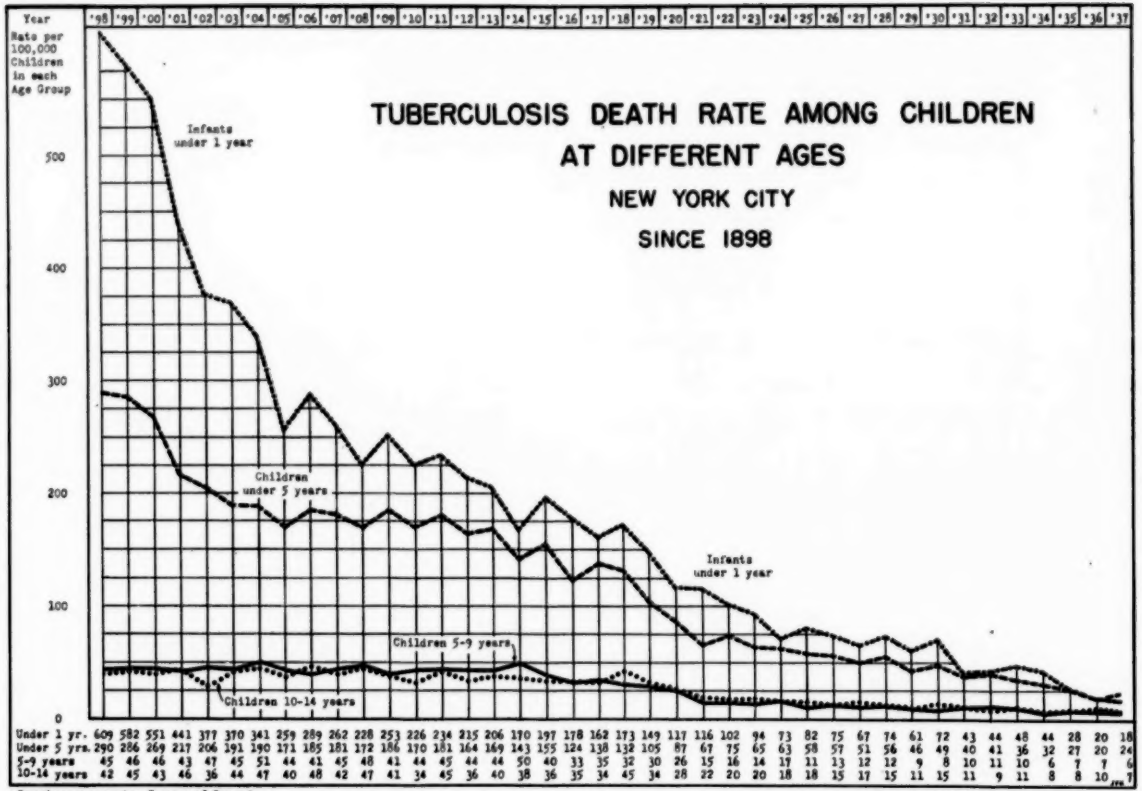

TUBERCULOSIS DEATH RATE AMONG CHILDREN
AT DIFFERENT AGES
NEW YORK CITY
SINCE 1898
Year
Rate per 100,000 Children in each Age Group
Infants under 1 year
Children under 5 years
Children 5-9 years
Children 10-14 years
Infants under 1 year
Based upon reports, Bureau of Records, Department of Health, City of New York.
G. J. Drolet, Statistician, New York Tuberculosis and Health Association, Inc.

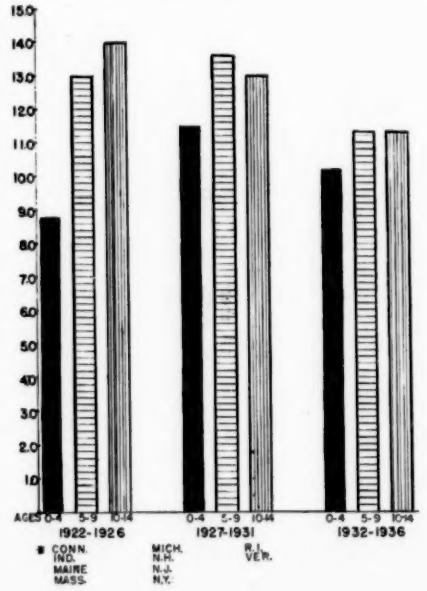
Chart 14.—This chart portrays another of the great accomplishments of preventive medicine and public health. The trend of this chart might suggest that tuberculosis is no longer a problem of major importance among infants and children. However, this is only relative, and reference to Charts 11 and 12 shows that much further improvement may be expected.

Chart 15.—It has already been seen (Chart 12) that appendicitis holds a prominent position as a cause of death in childhood. This chart suggests that there has been some reduction in the number of deaths from this cause in the older age groups during the past fifteen years. The apparent increase in the rates among children under 5 years of age may indicate only improvement in the recognition of the disease. Earlier recognition and prompt operation should, however, lead to a greatly reduced mortality at all ages.

Chart 16.—The prevention of deaths due to accidents is not primarily a medical problem, but the physician and surgeon can make substantial contributions toward this end. One might expect to find a high incidence of accidental deaths under one year and an increasing incidence among boys during the years of youth. The appreciable sex difference in the number of accidental deaths during infancy and early childhood, and the enormous discrepancy during the second decade would hardly have been anticipated.

TREND OF DEATHS FROM APPENDICITIS BY AGE AND BY FIVE YEAR-PERIODS

RATES PER 100,000 CHILDREN OF SPECIFIED AGES IN THE ORIGINAL TEN U.S.B.R. STATES*



DEATHS FROM VIOLENT AND ACCIDENTAL CAUSES BY AGE AND SEX—U.S.B.R.A.

AVERAGE NUMBER OF DEATHS PER YEAR 1933-1936 FOR EACH YEAR OF AGE

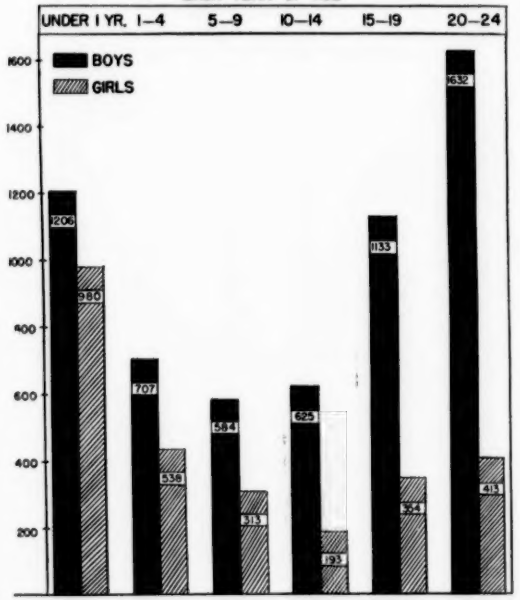


TABLE I

SUMMARY OF MORTALITY TRENDS FROM CERTAIN CAUSES IN A GROUP OF 42 STATES, 1934-38* (ESTIMATED POPULATION JULY 1, 1938, 116,400,000).† RATES PROVISIONAL FOR ALL YEARS

DISEASES (NUMBERS IN PARENTHESES ARE FROM THE INTERNATIONAL LIST OF CAUSES OF DEATH, FOURTH REVISION, 1929)	1938	1937	1936	1935	1934
	Rate per 1,000 population				
Deaths, all causes	10.5	11.1	11.4	10.9	11.0
Births, exclusive of stillbirths	17.0	16.5	16.2	16.4	16.5
	Rate per 1,000 live births				
Infant mortality (live births, 1938, 1,983,449)	48	52	55	54	59
Maternal mortality	4.0	4.5	5.2	5.5	5.6
	Death rate per 100,000 population				
Typhoid and paratyphoid fever (1, 2)	1.4	1.6	2.0	2.2	2.7
Measles (7)	2.4	.8	.8	3.0	4.5
Scarlet fever (8)	1.0	1.4	2.0	2.2	2.0
Whooping cough (9)	3.3	3.5	1.9	3.7	5.3
Diphtheria (10)	1.7	1.8	2.0	2.6	2.9
Influenza (11)	11.0	26.8	22.7	21.3	16.3
Poliomyelitis and polioencephalitis (16)	.3	1.0	.5	.8	.7
Encephalitis, epidemic or lethargic (17)	.6	.7	.6	.6	.7
Epidemic cerebrospinal meningitis (18)	.8	1.6	2.3	2.2	.9
Tuberculosis, all forms (23-32)	46.1	50.5	52.8	52.5	53.9
Malaria (38)	1.1	1.2	2.1	2.0	2.1
Pneumonia, all forms (107-109)	65.5	83.6	90.3	81.7	79.8
Diarrhea and enteritis under 2 years (119)	9.0	8.9	10.2	8.5	11.5
All accidents (176-195, 201-214)	70.0	79.5	85.5	78.7	80.7
Automobile accidents (206, 208, 210)	23.9	29.3	29.2	28.4	28.6

*The District of Columbia is included in this group and all states except Arizona, Arkansas, Louisiana, Mississippi, New Hampshire, New Mexico, and Texas.

†Populations used for the years 1934 to 1937, inclusive, are the official estimates as of July 1 of each year made by the Bureau of the Census. Estimates for 1938 are made by assuming the same actual increment between 1937 and 1938 as between 1936 and 1937 as given in the official estimates for those years. No official estimates for states are available for 1938.

The author is especially indebted to the Children's Bureau of the Department of Labor, the United States Public Health Service, the Massachusetts Department of Public Health, the New York Tuberculosis and Health Association, and the Department of Health of the City of New York for the opportunity to reproduce the following charts. In each instance the source of the material is indicated on the charts unless taken from the Reports of the United States Bureau of the Census.

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American Academy of Pediatrics

Proceedings

EIGHTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

DEL MONTE, CALIF., JUNE 9, 10, AND 11, 1938

Round Table Discussion on Aministration of Fluids

Chairman: Dr. Francis Scott Smyth, San Francisco, Calif.
Cochairmen: Hugh K. Berkley, Los Angeles, Calif.
John Mott Rector, San Francisco, Calif.

Fluid Administration

Francis Scott Smyth, M.D.

Introduction.—The problem of fluid administration involves these principles: An understanding of the assimilation, transportation, and elimination of fluid. The types of deficit—water, electrolyte, and colloid created by infection, or metabolic upset with or without impaired elimination and transport. The sites and types of administration. The dosage and the type of fluid to be given in relation to the need of the patient. I intend to introduce the subject by discussing the first two items—assimilation, transport and elimination—from the theoretical point of view. Dr. Rector will present the clinical application giving doses, technique, and cautions. Dr. Berkley will discuss the controversial feature of transfusion. I have prepared an exhibit which may be seen by those more interested after this session is over. The graphs you will probably recognize as those of Gambles "Chemical Anatomy."

Fluid Administration.—The importance of water in infant care was recognized by Hippocrates who observed, "Of sucklings they that pass much water are least inclined to illness."

Gross estimation of the water content of body tissues varies with the age of the individual. Pehme estimated the water content in ash- and fat-free tissues and found it to be:

90 per cent in a six months' fetus
84 per cent in an infant at term
82 per cent in a 3-year-old child,

while such tissues of an adult contained 76 per cent. Variation in water content is found between tissues, being much less in dense structures, such as bone, than in muscle and parenchymatous organs.

Compared with the adult the infant requires from two to three times as much fluid in proportion to weight. This may be explained by the relatively greater heat production of the young. If we assume that the water is eliminated 50 to 60 per cent by kidney, 30 to 35 per cent by skin and lung, and 5 to 10 per cent by way of the bowel, we find a scant 1 to 2 per cent retained. Factors which may increase the need of water or interfere with intake and output of water may seriously upset the infantile metabolism by quick depletion of reserves. Such factors as high external temperature, severe diarrhea, vomiting, and febrile infections, especially affecting the respiration (pneumonia), will increase the water loss.

I think it is safe to say that parenteral fluid administration has proved a life-saving procedure for many of those infants whose poor reserves were depleted in infection or abnormal loss beyond the point of oral restoration. However, more recently we have noted with concern the abuse of fluid administration where, without regard to the nature of the fluid or the deficit of the infant, the patient might be said to have been "drowned inwardly."

There is only one natural portal for the intake of fluid. Yet I believe there are occasions when, because of the ease of parenteral administration, the natural route may be neglected. For the most part the selection and adjustment for transport are much more readily accomplished when the fluid has been administered by the natural route. However, it must be admitted that some individuals—especially psychiatric patients—may ingest by mouth more fluid than can be readily assimilated. Perhaps the regurgitation of infants is their protection.

While there is but one natural entry for fluid, the channels of elimination are more numerous—kidney, bowel, skin, and respiratory tract. The kidney, as has been said, normally plays the major role in elimination. Damage or interference with its function will logically affect the fluid metabolism. Nephritis of the acute glomerular type may be characterized by acid phosphate retention, while another chronic pathology may with polyuria lead to a depletion of base due to the failure of the kidney to manufacture ammonia from urea as a base saver. The anuria of dehydration itself may be accompanied by phosphate and nitrogen retention, hence points to the vital importance of adequate water for renal function. Mention should be made that certain electrolytes tend to stimulate renal excretion of water, while others favor water retention.

We have said that physiologically the second important channel for fluid elimination is the intestinal tract. However, in enumeration of causes for dehydration in infants, the bowel probably ranks first. Anatomically the gastrointestinal tract is shorter, and functionally it is much more active in infants. For these reasons we expect considerably more wastage of fluid by way of the infant's bowel. The lability of the intestinal tract in young children is notorious, and we accept symptomatic vomiting and diarrhea as a frequently encountered symptom from disturbances remote from the tract itself. This peculiar lability makes for considerably more frequent use of parenteral fluid administration since fluid by mouth may be vomited or passed rapidly through the gut without absorption. By the same token, retention in rectal administration is often unsuccessful in young infants.

As with altered renal activity, so also with altered intestinal function one should be aware of changes in body fluid composition other than water loss. Vomiting, for example, usually is largely gastric in which instance there is a relatively greater loss of chloride ion as HCl. In this instance the water loss may be accompanied by a relative alkalosis. Where duodenal contents are also lost by vomiting, alkali such as sodium is also lost. In this latter instance both base and acid deficits may be found. Diarrhea represents a loss of water and both acid and base electrolytes. With normal peristalsis electrolytes would be reabsorbed in the colon. Their replacement with upset physiology is as much a problem as the replacement of the water itself.

The third important channel of elimination of water is the skin and respiratory tracts. In all likelihood the seasonal incidence of summer complaint is at least in part attributable to increased peripheral loss of water. In a more exaggerated form it is seen in miner's colic, and the recent work (e.g. at Boulder Dam) illustrates the importance of chloride as well as fluid restoration. I know of no work showing the necessity of guarding against chloride loss in infancy where only skin loss is concerned, but it is logical to suppose the problem exists. Fever, regardless of the cause, will increase peripheral evaporation as well as loss by way of the respiratory

tract. Where the fever is found with respiratory infection an even greater loss of fluid may be expected with the increased respiratory rate.

So far we have reviewed the intake and excretion of fluid. The transport and metabolism within the body are more complex. While obviously in part dependent on vascular and lymph channels as well as the pumping mechanism of the heart, the transport of fluid is not simply a matter of plumbing. In the finer ramifications of the vascular bed the capillary tension is balanced against the capacity of the serum protein to hold the water, i.e., the colloidal osmotic pressure or oncotic pressure. Body water is seen to consist of two systems: (1) the extracellular as in blood, lymph, and interstices between cells; and (2) the intracellular enclosed within cell membranes. Colloids and electrolytes differ in the two systems. Sodium and chloride are, for example, characteristic of the extracellular fluid while potassium and phosphorus are found within the cells. Obviously, diffusion and osmosis as through a semipermeable membrane accomplishes the transport to the cells themselves. When water and electrolyte are lost by the body, the first line of reserve, the plasma is affected. The interstitial fluid promptly replaces the deficit, and as this reserve fails we see the accustomed loss of elasticity to the skin, etc. Now while existing in equilibrium with the interstitial fluid, the fluid within the cells is not a reliable reserve. The water content may be reduced to the point of cell death but the differences in electrolyte allow no simple substitution of fluid from within the cell for that beyond the cell membrane.

It is obvious from what has already been said that successful administration of fluid depends on a recognition of electrolyte disturbance as well as of the deficit of water. Most of us have seen instances of diarrhea and oliguria treated for a long period with normal salt solution but with poor clinical response. In these cases the base-bicarbonate remains low, but the base strongly bound with chloride is elevated. For such cases sodium bicarbonate or lactate may be of considerable value. Dextrose solution alone is also of value but when such clinical conditions require fluid for long periods of time prolonged use of normal salt solution is contraindicated.

Considerable improvement in our methods has resulted from recognition of the role of colloids in the transport of fluid. For example with anemia from infection, malnutrition, or hemorrhage, a depletion of serum protein results in faulty transport of electrolyte and water. Transfusion, serum, and even acacia have been used with improvement as far as the fluid transport is concerned. It is my opinion that occasionally an anemia may be masked by the temporary concentration of cells in the blood and that occasionally instances of colloid deficit may occur without a marked cellular reduction. Plasma concentration by lyophile process may offer an ideal method and in the less acute stages some attention should be paid to a nutritional program for regeneration. This whole matter is, of course, controversial, and I hope Dr. Berkley will help clarify our views by discussing transfusions per se.

There remain instances of failure in absorption of fluids which are apparently not due to faulty electrolyte balance or failure of colloidal osmotic pressure. The report of Minot suggests that the edema which develops is due to damage to the capillaries which allows increased permeability with loss of serum protein and fluid. Casparis hints that there may be some fundamental mechanism involving the sympathetic-parasympathetic which controls capillary permeability and hence renal function. It is to be hoped that his investigations may lead to the use of drugs to correct autonomic imbalance. Even less well understood are the relationships with hormone control. Diabetes insipidus and Addison's disease leave no doubt as to their influence in fluid and electrolyte disposition. The peculiar selective secretion in Addison's disease and the results of chemical and hormone administration might be cited as an example. McLean suggested that suprarenal insufficiency was a cause for intestinal intoxication. It is at least wise to keep an open mind with regard to developments in this field.

Clinical Consideration of Fluid Administration

John Mott Rector, M.D.

Fluids are a very important item in the therapy of those patients in whom blood volume and rate of flow are diminished. Such conditions are found most frequently in feeble, malnourished, and dehydrated patients and in those suffering from acute, subacute, and prolonged infections, intoxications, metabolic disturbances, burns, hemorrhage, and severe trauma, both surgical and accidental. Blood transfusion should seldom be performed unless it is preceded or accompanied by other fluid parenterally.

The daily water requirement from birth to an age of 2 years is 150 c.c. per kilogram of body weight (2 ounces per pound). From 2 to 6 years, 100 c.c. per kilogram (1.5 ounces per pound), and thereafter 60 c.c. (1 ounce per pound) are needed. Older children should drink at least 1,000 c.c. (1 quart) of fluid daily. To restore normal fluid exchange in the presence of moderately severe dehydration about twice these amounts are required until the depleted fluids have been replenished. A seriously dehydrated patient has lost water amounting to 6-10 per cent of his body weight. If one-tenth of the body weight is administered in the form of fluid (100 c.c. per kilogram of body weight), it is usually adequate to supply lost water.

How often fluids should be repeated depends upon the condition of the child as a whole, and upon such specific matters as a drop in the fever, stabilization of the weight curve, improvement in the circulation, and diminution in fluid loss. Tissue turgor and urinary excretion are also useful clinical guides in determining the quantity and frequency of fluid administrations.

There is no question, of course, but that the ideal manner to give liquids is by mouth. Two special sensations were devised to insure an adequate maintenance of extracellular fluid (the plasma of the blood and the interstitial fluid, including lymph) —the sensation of thirst and a specific craving for sodium chloride. We should be careful to foster these and exhaust the possibilities of oral administration before recourse to parenteral routes.

Most infants, with judicious urging, will take water fairly well from a bottle, particularly when small amounts are offered at frequent intervals. Liberal dilution of the bottle feeding should not be neglected and offers the double advantage of reducing the ingestion of food and increasing the intake of water. As a rule, plain water is preferable although there is usually no objection to the addition of 5 per cent dextrose. At times large amounts of fluid can be given as diluted (strained) orange juice, other fruit juices seldom succeeding as well. Some infants prefer a salted water, made up as normal saline solution in half physiologic strength (0.42 per cent) with or without added dextrose, not infrequently tolerating a mixture of this kind when food or water cannot be retained.

In older children the variety of disguises in which water may be clothed is greater and with some ingenuity large amounts of liquid can be given. Fruit juices, clear broths, carbonated drinks, dilute nectar, weak tea, etc., may be used, depending upon the individual whims of the child. In the presence of nausea liquid should be chilled. With severe vomiting, the quantity that can be tolerated at one time may be only a teaspoonful initially, but even under these circumstances it is often possible to maintain a satisfactory water balance by the oral route alone. In acute illnesses it is rarely overdone.

If a child for any reason such as prematurity, weakness, nausea, profound sickness, or coma cannot take fluid in the usual manner, it may be administered by gavage, either oral or nasal. The former is preferable in small infants. Either procedure should be discontinued as soon as possible. The nasal drip method of gavage may be used to advantage if vomiting results whenever there is any considerable

quantity of liquid in the stomach at any one time. With a nasal catheter (No. 8-10 French) reaching to the midesophageal region, most infants will tolerate about 15 drops per minute, amounting to 50-75 c.c. an hour. A preceding gastric lavage is of value. Nasal tubes should be manipulated gently and not left in place more than half a day at a time to safeguard against the possibility of such complications as ulceration of the nares, rhinopharyngitis, otitis media or pneumonia, and fatal ulceration and edema of the esophagus.

In the presence of persistent vomiting the nasal drip method is often not satisfactory, and continuous duodenal drainage may be instituted to advantage. This is accomplished through a Levine tube (nasal catheter) attached to a gravity suction apparatus of the Wangensteen type. It is of particular value when there is marked abdominal distention, gastric dilatation, peritonitis, paralytic ileus or intestinal obstruction.

While the success of rectal fluid administration depends to a considerable extent on the degree of dehydration at the moment, this method is of limited use in childhood, especially in children under the age of 4 years. In older children fluid may sometimes be given rectally as a temporary or adjuvant measure. From 60 to 120 c.c. is injected slowly at four-hour intervals, depending upon the age of the patient and his retention ability. The Murphy drip is more often successful than the retention enema, flow being regulated to about 50 drops per minute. Tap water is the most suitable fluid, as normal saline (0.85 per cent) and 3 per cent sodium bicarbonate, formerly popular, do not favor rapid absorption because of their osmotic pressure; dextrose solutions are prone to cause abdominal distention.

When more rapid absorption of fluid is desirable, it may be administered by the subcutaneous, the intraperitoneal, or the intravenous route. The exact quantity to be given a child cannot be stated categorically but is determined roughly by a clinical judgment based on age, nutritional state, nature of the illness, tissue turgor, severity of vomiting and diarrhea, etc. The amount of fluid per kilogram of body weight found by experience to be effective is greatest in children under 1 year of age; the amount required relative to body weight decreases with age. While 150 c.c. of parenteral fluids per kilogram of body weight in twenty-four hours are usually safe amounts, not more than 20 c.c. per kilogram and a maximum total of 250 c.c. should be given at one treatment to infants under 2 years of age. Edema, water intoxication, circulatory embarrassment, and pneumonia may follow too much fluid.

Hypodermoclysis, especially in infancy, is very effective. Fluids well tolerated by the subcutaneous tissues are normal saline, Ringer's solution and all of its modifications, isotonic sodium lactate, and dextrose, either hypotonic or isotonic (5.5 per cent). Physiologic salt solution is most frequently employed. Although Ringer's and other solutions designed to imitate the electrolytes of blood plasma are used rather extensively, as a matter of practical experience normal saline usually proves quite effective. Dextrose solutions are indicated if ketosis is present. Sodium bicarbonate solution should not be given by hypodermoclysis. Favorite sites of injection include the loose tissues of the thighs, chest and back, administered by syringe in small infants and by gravity in larger ones. Dehydrated patients will usually absorb 50-80 c.c. of fluid per kilogram in this way and the treatment may be repeated in twelve to twenty-four hours, if necessary. Absorption is greatly enhanced if a simultaneous injection of hypertonic dextrose (10 per cent) solution is given intravenously. Reactions are rare, occasionally there is a transient rise in temperature. When sclerema is present, subcutaneous fluids are unsatisfactory. In the presence of dyspnea administration should be limited to the thighs. Because of the attending restlessness hypodermoclysis should be avoided in diphtheritic patients.

Infusions given intraperitoneally are absorbed more rapidly, but this method is rightfully on the wane as the procedure is unsound surgically and not without some danger. When used, it is essential that the infant be well immobilized and so restrained that the knees cannot be flexed. The solutions are the same as those recommended for hypodermoclysis with the exception of dextrose, which often produces abdominal distention. With a short bevelled, rather dull 16-20 gauge needle, 2 inches long, the fluid is given by gravity or syringe after the bladder has been emptied. The skin and peritoneum should be punctured in different places to minimize leakage. From 100 to 350 c.c. of fluid may be injected according to the size of the child. Overdistention of the abdomen is to be avoided, and the temperature of the solution should rather closely approximate that of the body to minimize symptoms of shock. The presence of pulmonary infections, abdominal distention, peritoneal adhesions, peritonitis, or impending laparotomy interdicts the procedure.

Of the various routes for administering parenteral fluids, the intravenous is eminently the most satisfactory. In presenting the role of intravenous therapy, however, it should be emphasized that the procedure can rarely be of much value unless carefully and skillfully executed; there must be little disturbance to the patient. The ease with which this operation is accomplished depends very largely upon individual technique and ability.

The veins of choice are the following: superficial temporal veins of the scalp, internal saphenous at the ankles, antecubital veins, dorsal veins of the hands and wrists, external jugular, and femoral veins. The scalp veins are usually most satisfactory in small infants and the antecubital veins in older children. The longitudinal sinus and the deep jugular vein are not recommended. Only rarely is it necessary to expose a vein. However, it is far preferable to "cut down" rather than to jeopardize a sick infant needlessly with a series of unduly prolonged and unsuccessful punctures. After carefully determining the vein most desirable for puncture, a needle suitable to that particular vein is selected and the child is restrained in good position. The needles are either hypodermic needles, 25 gauge, or platinum iridium needles, 18 to 22 gauge, 1¼ inch with a short, sharp bevel. It is much more convenient to have the needle attached to a syringe of the Luer-Kauffman type or a three-way stopcock. The site of operation is prepared, and, when scalp veins are used, the area is shaved. The operator scrubs, no sterile gloves or gown being necessary. Manual compression of the vein is superior to a tourniquet in small infants. The rate of flow should seldom exceed 10 c.c. per minute. It may be more accurately determined if the gravity flask consists of a graduated, 250 c.c. cylinder of small diameter. Concentrated solutions should be given more slowly than dilute ones. If injection has been too rapid, a chill and shock may follow. When small gauge needles are used, "milking" the tube will accelerate flow. Fluid to be administered should first be placed in warm water at a temperature of approximately 38° C. (100.4° F.) for ten minutes. It is equally important to keep the fluid warm by suitable means throughout the process of injection. If whole citrated blood is overheated before it is given, reactions are likely to occur.

An efficient apparatus for intravenous therapy in premature infants consists of an ordinary syringe of 50 c.c. capacity, attached to a rubber tubing about 18 inches in length, fitted with a Luer-Kauffman syringe. The large syringe serves as a receptacle, and fluid is administered by gravity. When necessary, an assistant replaces the barrel of the syringe and exerts enough positive pressure to insure a continuous flow.

The choice of solution must depend upon the individual case and at times is a matter of considerable moment. In the treatment of dehydration the immediate need is to restore the blood volume and reestablish renal secretion. This is effectively ac-

complished by the intravenous injection of hypertonic dextrose (10 per cent) in conjunction with normal saline or slightly hypotonic Ringer's solution subcutaneously. The resulting hydremia will usually cause a prompt resumption of urine secretion and since a normally functioning kidney can secrete acid or basic radicals as needed, either sodium or chlorine may be retained by the body and the other excreted in the urine. In this way either acidosis or alkalosis of moderate degree can often be remedied without the necessity of blood chemical determinations. In the immediate restoration of the circulation there is not much choice between physiologic saline and any of the various balanced salt solutions, which are really modified Ringer's and Locke's solutions. Ringer's solution probably has some advantage whenever there has been an unusual depletion of chlorides and the fixed bases, sodium, potassium, calcium, and magnesium. This is observed in such conditions as pyloric and intestinal obstruction, diarrhea, diabetic acidosis, the terminal stage of glomerular nephritis, and in many severe infections when large amounts of gastrointestinal secretions have been lost by vomiting or diarrhea. Ringer's solution is available in concentrated form as a stock solution which should be diluted twenty-five times (i.e., 10 c.c. to 250) with freshly distilled water before use. Ringer's solution should not be employed in the presence of sulfanilamide therapy because of its magnesium content.

Dextrose solutions are indicated when carbohydrate metabolism is low, when ketosis is present, and when depletion of liver or muscle glycogen exists, i.e., in conditions such as starvation, acute severe infections, hypoglycemia, and intoxications, particularly when affecting the liver and heart muscle. The addition of insulin is unnecessary except in diabetic acidosis. Hypertonic dextrose solutions are useful in promoting diuresis although corresponding concentrations of sucrose are superior when an actual dehydrating effect is indicated. The intravenous injection of 50 to 150 c.c. of 50 per cent sucrose solution is promptly followed by a prolonged diuresis and a corresponding reduction in cerebrospinal fluid pressure, unaccompanied by a secondary rise. When treating anhydremia, it is important to remember that dextrose solutions in concentrations greater than 5.5 per cent (isotonic), if given alone will increase dehydration. The commercial products available in ampoule form are quite satisfactory. After dilution, dextrose solutions become slightly acid upon standing and should not be kept longer than a few days.

In the prevention and treatment of disturbances in water and electrolyte balance of the acidotic type, a number of potentially alkaline solutions containing lactate can be used to advantage. They are also efficacious for rapid alkalinization of the urine in severe urinary tract infection. Gradual oxidation converts the lactate into bicarbonate, giving a rather prolonged effect without particular danger of alkalosis and tetany. Its action is independent of kidney function. Sodium lactate is marketed both in a concentrated form as molar sodium r-lactate which later may be diluted as desired, or in one-sixth molar concentration ready for administration. Lactate-Ringer's solution or Hartmann's "combined" solution consists of 10 c.c. of the molar sodium lactate in 450 c.c. of Ringer's solution. It is available commercially in 10 and 20 c.c. ampoules as physiological buffer solution. The "combined" solution is useful in combating cases of dehydration with moderate acidosis in patients in whom blood chemical studies have not been done. In the therapy of somewhat more severe acidosis (carbon dioxide content between 25 and 35 volumes per cent) "fortified" lactate-Ringer's solution is probably the fluid of choice. This is prepared by adding Ringer's solution to one-sixth molar sodium r-lactate solution in the ratio of 4:6, i.e., 40 c.c. of Ringer's to 60 c.c. of one-sixth molar lactate. Half of this may be given intravenously and the remainder subcutaneously. The dosage of sodium lactate depends upon body weight; 60 c.c. of one-sixth molar lactate or 100 c.c. of

"fortified" lactate-Ringer's solution per kilogram elevates the alkaline reserve about 35 volumes per cent. The addition of dextrose to any of these alkaline solutions is often advantageous, since it is best to mix isotonic solutions in equal volumes to preserve isotonicity.

Lactate therapy is open to one serious objection. In a certain number of these children with marked dehydration, the circulation is so poor that lactate is not oxidized and actually may be considerably increased in the blood; to give additional lactate under these circumstances would seem futile. In acute cases of this type it has been suggested that intoxication with guanidine may be the factor which impairs lactate metabolism. With any degree of liver damage lactate solutions are of doubtful value, and in the therapy of acidosis secondary to congestive heart disease with anoxemia lactate is contraindicated.

The treatment of severe acidosis (carbon dioxide content below 20-25 volumes per cent) calls for the intravenous administration of sodium bicarbonate if uniform results are to be expected. A freshly prepared, 4-5 per cent solution in distilled water is used. Should this be combined with dextrose solution immediate injection is essential as dextrose decomposes rapidly in the presence of alkali. Sodium bicarbonate solution cannot be mixed with Ringer's solution without precipitation of calcium bicarbonate. Dosage is based upon body weight. One gram of sodium bicarbonate per kilogram raises the carbon dioxide content about 40 volumes per cent. In the emergency treatment of acute acidosis where the carbon dioxide content is not known, it is usually safe to inject 17 c.c. of 4 per cent sodium bicarbonate solution for every kilogram (8 c.c. per pound) of body weight (i.e., 0.68 gram of sodium bicarbonate per kilogram). If renal damage exists, alkali therapy must be undertaken with caution. Care must also be exercised to replace lost plasma protein and chloride (transfusion), or else the latter may be retained in abnormal concentration.

In the presence of alkalosis a reduction in bicarbonate content with restoration of chloride and hemodilution may be effected either indirectly as a result of selective renal activity following normal saline solution (or Ringer's) or directly by the intravenous administration of a 5 per cent solution of hydrochloric acid in physiological salt solution in calculated amounts.* Acid therapy obviously acts with greater rapidity, but it is dangerous and, if used, should be reserved for cases with a carbon dioxide content over 90 volumes per cent. The injection should not be given faster than 3 c.c. of dilute solution per minute and is discontinued if hyperpnea develops. Tetany is best relieved by intravenous calcium chloride, in amounts of ¼ c.c. per kilogram, using a 5 per cent solution.

Intravenous acacia raises the colloidal osmotic or oncotic pressure and tends to maintain blood volume. In the form of a 6 per cent solution in 0.9 per cent sodium chloride it has been used considerably in the treatment of hemorrhage or shock but is inferior to citrated whole blood in these conditions. Because of the rapidity with which the proteins are excreted, acacia solutions have been advocated anew for the nephrotic syndrome. A dosage of 1 gram of acacia per kilogram of expected body weight produces a concentration of about 2 per cent of acacia in the blood plasma, which is equivalent in colloidal osmotic pressure to 1 per cent of serum albumin. The stock solution (30 per cent acacia with 4.5 per cent sodium chloride) is usually diluted with two parts of distilled water for administration. Injections are given at two- or three-day intervals and should not exceed four in number, as acacia accumulates in the liver and spleen and is toxic. In nephrosis the results from acacia therapy, as measured by diuresis, dissipation of edema, and plasma protein effect,

*Calculation of acid dosage: c.c. con'c. HCl = vol. per cent CO_2 excess (over 70) × 0.028 × wt. (kg.).

have not been uniform, even in patients with no apparent renal insufficiency. Severe reactions, so frequently observed after these infusions, have further militated against the use of this product. Acacia solution is incompatible with sodium bicarbonate and with citrated whole blood.

Magnesium sulphate in 2 per cent solution intravenously is of benefit in conditions associated with hypertension, particularly of the convulsive type as in nephritis with uremia. The dose varies according to individual response and the degree of hypertension present. Frequent blood pressure determinations are made throughout the injection, which is discontinued after a judicious drop has been obtained. For the convulsions of tetany intramuscular magnesium sulphate is preferable, a 25 per cent solution in amounts of 1 c.c. per kilogram. As respiratory depression occasionally occurs with this drug, it is customary to keep calcium chloride on hand for counteraction.

The amount of fluid that can be given at one time intravenously is limited owing to the danger of overloading the circulation. If repeated injections are necessary, it is frequently desirable to administer fluids by continuous drip. Contraindications are the failing heart, pulmonary congestion, hypertension, and nephritis. Various methods and many modifications have been devised for this type of intravenous therapy. One of the most simple and effective is the use of a gravity apparatus with a modified Murphy drip attachment. The needle, a 22-24 gauge with its beveled point cut off, is inserted securely into a piece of sterile No. 4 ureteral catheter about three inches long. The veins of choice are those of the arm and ankle. After careful fixation of the part with a padded posterior splint, the vein is exposed surgically through a small skin incision and tied peripherally with a catgut ligature. It is then partially cut above with a fine scissors, and the ureteral catheter is inserted and tied in place. If warm saline solution is allowed to drip on the vein while the catheter is being inserted, sufficient dilatation will occur to expedite the procedure materially. The fluid, as it enters the vein, should be maintained at approximately body temperature, and the rate of flow must be carefully regulated. After immediate dehydration has been relieved, a rate of 15-20 drops per minute (3-6 c.c. per kilogram) is usually satisfactory. More rapid injection may result in temperature elevation and chills, glycosuria, edema, and embarrassment of the circulation. Isotonic dextrose (5 per cent) in Ringer's or Hartmann's solution is recommended. The judgment of the physician must determine the balance between too little and too much fluid. The principal evil lies in its abuse. The total fluid, included in the diet and given as liquid by mouth and parenterally, should not exceed 150 to 180 c.c. per kilogram of body weight per day. If there is any sign of edema, pulmonary or otherwise, the amount is reduced. Continuous intravenous therapy is rarely required after the third day. A good working rule is to remove the needle after seventy-two hours and if necessary use another vein later. If there is a cessation of flow, the apparatus should not be dissembled without due thought of the possibility of air embolism. When dextrose is employed, tenderness and redness along the course of the vein from a chemical phlebitis may appear; this rapidly subsides when treatment is discontinued.

The continuous intravenous drip method of forced spinal fluid (perivascular) drainage is becoming increasingly popular. A hypotonic (0.45 per cent) buffered salt solution is given at a rate sufficient to maintain a steady flow of spinal fluid (about 20 c.c. of hypotonic saline per kilogram per hour). Headache, nausea, chills, or convulsions necessitate temporary interruption of forced drainage. The procedure is contraindicated in cardiovascular-renal diseases, encysted or encapsulated fluid accumulation in brain and cord, and acute or chronic infections elsewhere in the body.

While most infusion fluids may be said to be safe, occasionally a febrile reaction, or series of reactions, occurs. The factors alleged to cause these are mostly the result of conjecture. It appears, however, that such things as pH of fluid, impurities in glassware and rubber tubing, etc., play some part, but most reactions arise from pyrogenic fluids. If distilled water is pyrogen-free, trouble will rarely ensue.

Dangers incident to excessive fluids have frequently been described, and fatal complications have been recorded. Symptoms of so-called water intoxication include nausea, vomiting, headache, vertigo, increased blood pressure, muscular pain and twitching, convulsions, coma, and death. While water retention and varying amounts of hemodilution occur, the striking feature is a reduction in extracellular electrolytes, especially chlorides. The mechanism in these cases is not clear; individual susceptibility may be a contributory factor. Experimentally, it has been demonstrated that injury to the hypophysis or to the adrenal cortex definitely predisposes to a state of water intoxication; this can be prevented by the administration of cortin and is amenable to the intravenous injection of hypertonic salt solution (5 per cent).

Rather analogous are those paradoxical cases of dehydrated children who are unable to utilize parenteral fluid in a normal manner. In anhydremic patients with extensive burns, for example, there is likely to be some adrenal cortex injury, and in these patients one frequently finds a severe hemoconcentration that persists in spite of abundant fluids intravenously; instead of being used to redilute the blood, fluid is shifted to extravascular depots, and a condition of actual water retention obtains. After using adrenal extracts in these cases for several years, it is my clinical impression that their adjunct use in large doses will assist in the maintenance of a more normal fluid exchange.

Transfusions

Hugh K. Berkley, M.D.

Our remarks on transfusions are based, for the most part, on experiences encountered during the past ten years at the Children's Hospital in Los Angeles. Ideas, methods, and even deductions vary widely from time to time in the practice of medicine. Practices considered standard ten or even five years ago are today antiquated or obsolete. This is certainly true of transfusions, the methods of giving them, the reasons for which they are given and, we believe also, in the interpretations of the results obtained.

It seems necessary to preface my remarks for today in this manner. Otherwise some of the statements might be understood as criticisms of the work which was done at the time it was done. As a matter of fact, I am not critical in that sense but in the sense that now we may look back and see errors to which we were at the time quite blind. During the next ten years methods presently acceptable may become obsolete.

I desire that none of the remarks be taken as critical of the individuals doing the work nor of the hospital in which the work was done. I believe, in fact, that most individuals and most hospitals would present data similarly vulnerable to analysis.

For practical considerations transfusions at the Children's Hospital were begun in 1931. Obviously this arbitrary date is not the date of the first transfusion. From a modest beginning there was a steady increase in the number performed each year, reaching a maximum in 1936. Most of the increase occurred on the medical service. In a period of ten years the total number of transfusions has reached 1,800.

The indications for these transfusions have been many and varied. Many of the indications, at the time seemingly justified, would today be classed as unjustifiable. For example, who today would recommend a transfusion for a simple iron anemia

or for acrodynia? And yet even today we are guilty voluntarily or involuntarily of almost as inexcusible practices. In this year I permitted a patient with an acute lymphatic leucemia to be transfused four times at great inconvenience to the child and a considerable expense to the parents only because they were determined to keep him alive as long as possible in the faint hope that someone, somewhere, might discover a cure for the disease while he still lived.

Thus it is wise that we be tolerant when we find transfusions given for conditions not now on the accredited list. By experience we learn.

Our list shows transfusions given for acute hemorrhage, chronic hemorrhage, all forms of blood dyscrasias such as leucemias, hemophilia, idiopathic and symptomatic purpuras, anemias of the various forms both acute and chronic, septicemia, sepsis, local infections, pneumonia, emphysema, meningitis, peritonitis, preoperative support, postoperative support, inanition, marasmus, athrepsia, acrodynia, etc. Many have been done simply as a "boost."

Sanction of some of these indications would be difficult today. But difficult as this might be, it seems still more difficult, to the writer, to enumerate a list containing only those conditions where transfusions may be now considered of essential value. One might easily subscribe to the idea that transfusions were of value in replacing blood loss and for the specific or nonspecific antibodies present in the transfused blood.

Clinical observations, not capable of accurate analysis or measurement, still point to the fact that transfusions are valuable over a broader field than this. Clinically transfusions seem definitely valuable in instances where no laboratory method now used can demonstrate the reasons for their effectiveness.

To transfuse or to not transfuse must still be left to the judgment of the individual physician and the success or failure of the effort will, in the last analysis, rest on the keenness of his decision.

Methods Used.—To maintain a high degree of efficiency in the procedure of transfusion, we have, at the Children's Hospital, established a transfusion team. For a given period of time all transfusions are performed by this team. Replacements on the team are made in a staggering fashion so that one experienced operator is always on hand.

Early in our experience more or less severe reactions frequently occurred during or soon after the transfusion. Investigation revealed this to be due to pyrogens developed in the water used. Electrical tests revealed a conductivity of 33 moles in place of the desired 3 moles. Fractioned, double-distilled water removed this difficulty.

All glassware is especially selected and cleaned. All tubing is pure gum and is especially cleansed. All rinsing solutions are of the same water as is used in intravenous solutions.

Blood groupings are done according to the Moss classification. After typing the patient and the donor, the bloods are cross-matched just prior to the operation. Cross-matchings of the day before transfusion are not accepted. A given donor is never used more than twice on the same patient.

Until recently most of our transfusions have been by the direct, multiple syringe method with saline or citrate solution being used only for rinsing a syringe before a refill. This procedure has certain disadvantages in infants and young children. The veins in these patients, at best, are small, and in patients requiring transfusion they are often very small, making a cut-down necessary. Needles of small caliber must be used and in giving large amounts of blood, clotting is likely to occur. If considerable speed is used to prevent clotting, the small, fragile veins often rupture from the pressure exerted. If one survives these two hazards, a patient with

respiratory difficulties may suffer from pulmonary congestion due to the rapid increase in pressure. In such an event the transfusion must be discontinued entirely or slowed down to a point where clotting again becomes a problem.

During the present year 60 per cent of the transfusions have been performed by the indirect citrate method. Multiple syringes may be used, but marked preference is now given to the Baxter vacoliter apparatus. About 10 per cent of a 2.5 per cent solution of sterile sodium citrate is added to the blood as an anticoagulant. This having been done, the suction portion of the apparatus is replaced by the delivery tube; the bottle is turned upside down, and the needle inserted in the vein of the recipient. Because of the anticoagulant, speed is no factor either in getting the flow started or in the rate of flow after starting. In fact, the blood may be allowed to flow at the same rate and in the same manner as a continuous drip, or hurried along to the full capacity of the needle.

Much controversy has arisen over the ill effects attending the use of sodium citrate. Some of these criticisms are no doubt justified; many probably are not.

Calcium mobilization has been noted in our series, a mild form of tetany developing when the citrated blood was given rapidly. By decreasing the flow the signs of tetany usually disappear by the time the transfusion is completed. The simplicity and the convenience of the method seem at present to outweigh most of the theoretical objections to the method.

Prior to the described method of using citrated blood, 95 per cent of our transfusions required cut-down operations. Very few cut-downs are not necessary though they still are essential in certain instances, for example thin, emaciated and dehydrated infants. When as many as 55 transfusions have been given one child, the omission of a cut-down is a great help.

Contrary to the practice of many hospitals, we employ an oblique rather than a horizontal incision. This incision allows for more working space along the length of the vein and does not increase the difficulty of finding the vein. Incisions are rarely over ¼ to ⅜ of an inch in length. The veins used in cut-downs are not tied off and may be used again subsequently.

In any large series of transfusions certain accidents are bound to occur. Some of the accidents are of a more or less minor nature such as blocking of needles, rupture of veins, extravasations of blood, hyperpyrexia due to faulty solutions, chills, and allergic phenomena perhaps produced by not using fasting donors, hypertransfusion reactions, etc. Of these we have probably had our full share. Many of these will probably not recur because of continuous improvement in solutions and technique.

During the period between the years 1928 and 1938, we had 24 deaths which are believed to have been directly due to the transfusion. Careful scrutiny of these fatalities reveals the fact that for the most part the difficulty is due to a failure of judgment rather than to an error in technique. In some instances neither judgment nor technique is at fault but rather some unknown and uncontrolled factors which will require further study before they can be fully understood and perhaps thereby be avoided.

Eleven of the 24 deaths occurred in pneumonia patients who died of acute cardiac failure either during or immediately after transfusion. We believe these deaths were due to errors in judgment. This experience should make us all apprehensive when a transfusion is being considered in a case of pneumonia.

Anemia, or lack of blood volume, is rarely a problem in pneumonia. The patient is suffering much more from toxemia or perhaps from anoxemia. If from anoxemia, oxygen is the remedy. For toxemia, blood may conceivably be of value as an antitoxic agent. If so, it must be given in some volume to be effective. To increase the

blood volume materially in a patient, in most instances, already suffering from cardiac embarrassment, may add just enough extra load to produce an acute and fatal cardiac failure. Moreover, the use of other more diffusible fluids, such as glucose or glucose and saline, is equally if not more effective in reducing the toxemia.

Admittedly, when confronted with a patient very ill with pneumonia and seemingly going from bad to worse, there is a great urge on the part of relatives and in the mind of the physician to do something. A transfusion is a psychologically spectacular answer to this urge, but we believe, from our experience, that it is rarely, if ever, good therapy, and often most harmful. It should be added that type-specific antisera are available for certain pneumonias, and when available they should be utilized in preference to transfusions.

Of these 11 pneumonia fatalities, 9 were believed to be due to "speed shock." As has been pointed out, when using the multiple syringe direct method, speed is an important factor in successful technique. Two hundred or 300 c.c. of blood are often given in as little as 5 or 10 minutes. This hazard of speed can be wholly eliminated by the citrate method. Nevertheless, we still feel that transfusions in pneumonia may be, and often are, worse than useless.

Two patients died in acute asthmatic attacks, in each instance there being no history of previous allergic manifestations. It seems impossible to avoid this type of disaster. A more searching inquiry into the history and the use of fasting donors may be of some help.

Two patients died of acute renal insufficiency. Experimental evidence is available that this is due to the precipitation of large quantities of hemoglobin in the tubules of the kidney. In animals (dogs) this occurs only in the presence of an alkaline urine. Making certain that the urine is acid prior to transfusion may eliminate this type of accident.

Two deaths were produced by pulmonary emboli and one by a cerebral embolus. In each instance these transfusions were being given through the needle of a previously running intravenous drip. It seems therefore certain that, when a needle has been in place in a vein over a period of time, soft clots form around the needle. As long as these are not disturbed by handling, no harm results. In our experience needles have been in place and continuously delivering aqueous solutions over periods of five or six days without difficulty. However, when the needle is handled roughly, as it usually must be in making the change over to the transfusion apparatus, these clots break loose and, if they are of sufficient size, cause death. It is therefore evident that this procedure should never be used.

There has been one instance of what has been described as an anaphylactoid phenomenon, with agglutination of the red cells, perivascular edema, hemorrhage and congestion of various tissues of the body, particularly the kidney, the lungs, and the brain. It may be added that we have experienced one other death of this type where glucose and normal saline were being administered by continuous drip. The mechanism of this difficulty is not yet clear, but it may be related to that process which precipitates the hemoglobin in the kidney and which has been previously mentioned.

In five instances death followed extremely high temperatures which occurred immediately after the transfusion. The cause of these reactions still remains unknown.

Two patients died because of errors in matching bloods. There would seem to be no excuse for this type of accident. Because of the ever present human frailty—carelessness—an occasional fatality will probably continue to occur.

The remaining death occurred when a misguided house officer endeavored to transfuse into the radial artery. A fatal, massive hemorrhage was the unfortunate and unforgettable result.

We would like to call attention to certain other factors, of some importance, in relation to transfusions.

In all cases there is a definite drop in the reticulocyte count after a transfusion. This is due to a depressor effect on the red blood cell production organs.

In many instances there has been a serious drop in the number of white blood cells, chiefly at the expense of the neutrophiles. In some instances this has led to an agranulocytosis with ulcerative gingivitis and death. For these reasons the depressant action of a transfusion on the hematopoietic system must be constantly borne in mind.

Two other hazards of transfusions have been brought out in our cases. In two instances clinical malaria has been transmitted. Also two instances have occurred where patients have been transfused from seropositive donors, in each instance, fortunately, without the development of syphilis in the recipient.

The work of Cadham brings out certain points that seem most pertinent to the discussion of transfusions. So often transfusions are resorted to in the treatment of severe infections, especially cases of septicemia. His work shows that in most of these cases there is a marked reduction in the complement value in the patient's serum. A small amount of complement given to these patients is capable of reactivating their own complement to a remarkable degree. It seems at least possible, if not probable, that small complement transfusions might often and perhaps with more benefit be given in place of whole blood. A deficient factor in the patient's blood would thereby be replaced with a minimum of risk. Further, the same possible antibodies would be transferred as are transferred with whole blood. An additional and desirable factor is that complement apparently does not depress the hematopoietic system as always happens with whole blood.

Experience leads us to believe that the intravenous use of a 50 per cent glucose solution is more efficacious than transfusions in the treatment of shock.

With increasingly satisfactory results, aqueous solutions are gradually replacing the use of transfusions in our marasmus cases. It seems probable that they will, eventually, entirely replace them.

The process of blood transfer is a complicated mechanism. Because it is now easily accomplished, transfusions have been recommended and given far too frequently. In its proper place a transfusion is a great step forward in therapy. That we will continue to do them is certain. That we will do less of them in the future than in the past seems probable. Many unknown factors still surround their use, and much work is yet to be done before we fully understand their full advantages as well as their disadvantages.

DISCUSSION

DR. SAMUEL G. HENRICKE (PORTLAND, ORE.).—What experience have you had in giving small amounts of blood in repeated small transfusions intraperitoneally?

DR. BERKLEY.—The intraperitoneal route is used less frequently at present.

DR. LANGLEY PORTER (SAN FRANCISCO).—Are there any specific dangers which may be encountered from use of intraperitoneal transfusions?

DR. BERKLEY.—We should not forget the necessity for typing and matching blood before giving intraperitoneal transfusions.

DR. T. B. COOLEY (DETROIT).—The difficulty with intraperitoneal transfusion is the poor absorption of the blood. Feeble babies do not utilize the intraperitoneally administered blood.

CHAIRMAN SMYTH.—Would you prefer intramuscular to intraperitoneal administration of blood?

DR. COOLEY.—I should just as soon use serum or blood intramuscularly.

DR. EDWARD S. BABCOCK (SACRAMENTO, CALIF.).—I have given a great many intraperitoneal transfusions of blood with very good results and no trouble.

DR. LOUIS M. EARLE (HOLLYWOOD, CALIF.).—In a case where a mistaken diagnosis of leucemia was made, frequent transfusions were employed and recovery occurred.

DR. PHILLIP J. HOWARD (DETROIT).—How about transfusions in pneumonia? We frequently use the citrated and indirect method giving small and repeated transfusions of not more than 40 c.c. In patients whose hemoglobin is 8 gm. or below or who have less than 3½ million red blood cells it would seem well to replenish their blood.

CHAIRMAN SMYTH.—We are rather timid about giving blood in pneumonia, but rely on oxygen.

DR. C. I. MEAD (BAKERSFIELD, CALIF.).—In our community we have frequent outbreaks of gastrointestinal intoxication, and we use blood transfusion with good results in these cases.

DR. BERKLEY.—Blood banks when established at hospitals will allow its preservation for 30 days.

DR. COOLEY.—Why did you limit the time for storing blood to 1 week?

DR. RECTOR.—I have notice hemolysis in some instances after that time.

DR. HARRY BAKWIN (NEW YORK, N. Y.).—What is the objection to hemolyzed blood?

DR. RECTOR.—The use of hemolyzed blood causes febrile reactions.

DR. GEORGE PINESS (LOS ANGELES, CALIF.).—I think that some of these reactions are anaphylactoid reactions. According to the definition of Hanzlik, when fluid is given too rapidly we may overburden the right side of the heart. These reactions are totally different from true anaphylaxis and are nonprotein in character.

DR. PORTER.—In those patients who died of asthmatic attacks during transfusion, was there a previous history of allergy?

DR. BERKLEY.—They were not known to be allergic and gave no allergic history.

DR. PINESS.—I am inclined to believe that these were anaphylactoid rather than anaphylactic deaths. The only asthma that I have seen with transfusion occurred 24 hours after a second transfusion from the same donor.

DR. BRET RATNER (NEW YORK, N. Y.).—Can't you conceive of a child, sensitive to egg, receiving blood from a donor who had previously taken an eggnog, showing such an asthmatic reaction?

DR. PINESS.—Yes, but the pathologic findings reported were not typical of true anaphylaxis.

DR. BERKLEY.—The serum of a patient with Gaucher's disease who had been frequently transfused finally agglutinated all types of donors' cells.

DR. RECTOR.—In extremely septic children who exhibit the phenomenon of autoagglutination, the blood should be given slowly.

CHAIRMAN SMYTH.—Does the previous use of intravenous fluids aid in blood transfusions, that is do you think it might decrease any possible kidney damage?

DR. BERKLEY.—I feel that it is of value.

CHAIRMAN SMYTH.—Are you using transfusion frequently in conjunction with sulfanilamide?

DR. BERKLEY.—I think this is an individual indication. The use of the barbiturates as sedatives before transfusion is very helpful.

DR. JAMES W. BRUCE (LOUISVILLE, KY.).—Could you give more detail as to the technique for giving intravenous clysis?

CHAIRMAN SMYTH.—A detailed description of this technique was given.

DR. A. GRAEME MITCHELL (CINCINNATI, OHIO).—In cases of severe acidosis, I feel that frequent CO_2 determinations should be stressed.

CHAIRMAN SMYTH.—We should check the CO_2 simultaneously with the chlorides of the blood.

DR. BAKWIN.—Is the lactate excreted in the urine?

CHAIRMAN SMYTH.—We have not encountered frequent cases of dehydration in San Francisco. Our cases are associated with dysentery infections.

DR. BAKWIN.—We see cases in convalescence with a high blood chloride but a low proteinemia.

CHAIRMAN SMYTH.—The use of sodium bicarbonate in severe acidosis may be extremely valuable when given intravenously, especially, where the base-bicarbonate is low, around 12 to 15 per cent.

DR. S. R. KALISKI (SAN ANTONIO, TEXAS).—Do you feel that lactate-Ringer's solution is well adapted for the patient in whom chemical examination is not possible?

DR. BAKWIN.—Continuous clysis is more simple than continuous intravenous drip and can be more simply used. We do not give water by mouth until the babies are atoxic for two to four days. In this way a rest is given the intestinal tract.

DR. MITCHELL.—What about the danger of giving too much fluid?

CHAIRMAN SMYTH.—Dr. Rector has mentioned the danger of internal drowning and has given the approximate doses of fluid per pound of body weight.

DR. KALISKI.—So many children who have diarrhea are also vomiting that this latter symptom might give a clinical basis for the detection and treatment of alkalosis.

DR. JEFFERSON R. LEMMON (AMARILLO, TEXAS).—In children with intestinal intoxication and vomiting I have successfully used lactate-Ringer's solution, sometimes, with 5 per cent glucose, intravenously and by hypodermoclysis. I have also used the lactate-Ringer's solution intraperitoneally.

DR. OSCAR REISS (LOS ANGELES).—We have had rather shocking results at Los Angeles General Hospital with the use of intravenous acacia and hesitate to use it.

DR. HOWARD.—Our experience with acacia intravenously agrees with that expressed here; its usage does not seem advisable.

DR. JAS. ROSENFELD (PORTLAND, ORE.).—How serious is abdominal distention with the use of rectal injections?

DR. RECTOR.—In our experience abdominal distention is not a pertinent factor unless dextrose solutions are administered.

CHAIRMAN SMYTH.—Rectal injections too often act as an enema.

DR. ROSENFELD.—Because of the frequent irritability associated with intravenous injections, I frequently give a so-called high enema.

DR. BERKLEY.—I frequently give 1 to 2 ounces of either tap water or karo solution as an enema with complete satisfaction.

DR. RANDOLPH G. FLOOD (SAN FRANCISCO).—As a rule I feel that children sick enough for intravenous injections should be in a hospital.

DR. LYNN B. VAUGHAN (LONG BEACH, CALIF.).—Is there any danger in giving glucose solution under the skin?

CHAIRMAN SMYTH.—We have used a 3 per cent solution under the skin with satisfaction but no stronger solution.

DR. HOWARD.—How about giving insulin in the glucose? We have given enough insulin to burn one half of the glucose.

CHAIRMAN SMYTH.—We now use glucose exclusively, and in our experience it is not necessary to add any insulin.

DR. FLOOD.—Does not the use of hypertonic glucose solution result in depletion of the fixed bases?

DR. RECTOR.—The use of 50 per cent dextrose is extremely valuable in cases of shock and acute cardiac failure. Do not use plain water to dilute the glucose but dilute with a basic solution.

CHAIRMAN SMYTH.—We use hypertonic glucose only for the purpose of dehydration.

Secretaries

ARTHUR F. ABT, M.D., Chicago, Ill.
FRANK H. DOUGLASS, M.D., Seattle, Wash.

MEETING OF THE EXECUTIVE BOARD OF THE AMERICAN ACADEMY OF PEDIATRICS

Minutes of the Meeting of the Executive Board, held at the Orrington Hotel, Evanston, Ill., June 17, 1939.

The following were present:

Vice-president: Dr. Joseph B. Bilderback
Secretary-treasurer: Dr. Clifford G. Grulee
Regional chairmen: Region I—Dr. Stanley Nichols
Region II—Dr. E. C. Mitchell
Region III—Dr. A. Graeme Mitchell
Region IV—Dr. Edward B. Shaw
Associate chairmen:
Region I—Dr. Lewis Webb Hill
Region III—Dr. Edgar E. Martmer
Region IV—Dr. Hugh Berkley

In the absence of the president, Dr. Henry F. Helmholz, Dr. Grulee presided.

The following applicants were elected to fellowship:

Region I

Dr. James M. Baty, Boston, Mass.
Dr. Harry D. Bowman, Hagerstown, Md.
Dr. Abe S. Brown, Waterbury, Conn.
Dr. Fred T. Cavanaugh, Troy, N. Y.
Dr. Stanley S. Freedman, Providence, R. I.
Dr. George C. Glass, Hartford, Conn.
Dr. Paul Harper, Bridgeport, Conn.
Dr. Frank Jay Jacobson, Providence, R. I.
Dr. Spencer E. Levin, Boston, Mass.
Dr. Morris Y. Krosnick, New Haven, Conn.
Dr. Francis C. McDonald, Stoneham, Mass.
Dr. John McK. Mitchell, Rosemont, Pa.
Dr. Donald D. Posson, Rochester, N. Y.
Dr. Charles E. Turcot, Quebec, Que.
Dr. William R. Wilson, New Haven, Conn.
Dr. James J. York, Schenectady, N. Y.

Region II

Dr. Byron Alexander, Electric Mills, Miss.
Dr. Ben Andres, Longview, Texas
Dr. Francis A. Garbade, Galveston, Texas
Dr. Stanley G. Wolfe, Shreveport, La.

Region III

Dr. Edward J. Denenholz, Chicago, Ill.
Dr. Carl J. Ochs, Cincinnati, Ohio
Dr. G. E. Robertson, Omaha, Neb.
Dr. Walter J. Siemsen, Chicago, Ill.
Dr. Ralph Spaeth, Chicago, Ill.
Dr. Robert L. Wilder, Minneapolis, Minn.

Region IV

Dr. Milo B. Brooks, West Los Angeles, Calif.
Dr. Henry F. Gallagher, Los Angeles, Calif.
Dr. Berryman Green, Riverside, Calif.
Dr. Russell W. Mapes, Beverly Hills, Calif.

The resignations of Dr. Ray C. Armstrong of Champaign, Ill., and Dr. T. D. Walker, Jr., of Newport News, Va., were accepted and provisions made for their reinstatement if desired. The resignation of Dr. J. B. Phillips of Chattanooga, Tennessee, was accepted.

Dr. Walter D. Ludlum, Brooklyn, N. Y., was transferred from active to emeritus fellowship.

The Executive Board took definite action for any delinquency in dues of a year's standing, that for members so delinquent, the Academy would not pay the subscription to the JOURNAL and hence they would be taken from the rolls of the JOURNAL until the dues were paid.

Report of the Treasurer

Statement of Receipts and Disbursements

July 1, 1938 to June 30, 1939

BALANCE, July 1, 1938			$ 6,188.65
Transferred from savings accounts			
State Bank and Trust Co., Evanston		$ 8,000.00	
First National Bank, Evanston		5,000.00	
Sold—$5,000 City of Chicago Municipal T. B. Sanitarium Tax Anticipation Warrants 2¾% 1937 Levy		5,123.00	18,123.00
RECEIPTS			
Dues	$24,530.09		
International Congress	5,765.00		
Exhibits	2,240.00		
Interest	483.08		
Pamphlets on Immunization Procedures	83.50		33,101.67
			$57,413.32
DISBURSEMENTS			
The Northern Trust Company		$16,000.00	
International Congress of Pediatrics		5,560.00	
Salaries: Secretary	$ 6,500.00		
Stenographer	2,000.00		
Office	480.00	8,980.00	
Rent		600.00	
Subscriptions to Journal		6,221.62	
Publicity		2,034.47	
Executive Board		2,355.73	
Printing and stationery		802.89	
Annual meeting—1938	694.91		
1939	60.28	755.19	
Travelling expense		716.82	
Postage		568.84	
Insurance		62.50	
Office supplies		61.50	
Exchange and charge on checks		56.62	
Telephone and telegrams		50.13	
Certificates		20.00	
Refunds—Initiation fees		75.00	
Miscellaneous		76.30	

Regional Expense:				
Region I		303.86		
II		237.25		
III		77.82		
IV		105.00	$ 723.93	
State Expense:				
Region I				
Connecticut	$ 5.00			
District of Columbia	9.20			
New Jersey	31.73			
New York	78.62			
Rhode Island	2.22			
Quebec	2.00	$ 128.77		
Region II				
Arkansas	$ 10.00			
Florida	16.40			
Georgia	1.00			
Kentucky	3.00			
Louisiana	8.25			
North Carolina	10.00			
Oklahoma	12.50			
South Carolina	15.00			
Tennessee	15.65			
Texas	2.00			
West Virginia	3.34	$ 97.14		
Region III				
Illinois	$124.54			
Michigan	11.35			
Missouri	5.00			
Ohio	16.45			
South Dakota	2.00			
Wisconsin	6.32			
Meeting of State Chairmen	$391.91	$ 557.57		
Region IV				
Arizona	6.00			
California	18.00			
Washington	26.00	$ 50.00	$ 833.48	
Committees:				
Contact Infections		$ 83.61		
Mental Hygiene		109.50		
Neonatal Morbidity and Mortality		74.87		
Nonmedical Groups		296.28		
Medical Supervision of Camps		$ 10.83	$ 575.09	$47,130.11
Balance, June 30, 1939				$10,283.21

A general discussion regarding the annual meeting was held and many suggestions were offered.

It was decided that the Statler Hotel, Boston, Mass., should be designated the official headquarters of the American Academy of Pediatrics for the International Congress of Pediatrics.

The report on publicity from Mr. Lawrence H. Selz was received. The Executive Board voted to thank Mr. Selz for an excellent piece of work and to commend him not only for his efficiency, but also for his interest in the Academy.

Region I.—The next meeting of Region I will be held in Washington, D. C., April 4, 5, 6, 1940.

Dr. Stanley Nichols reported many activities, among them being the active interest which the Academy members in New England were taking in the New England Pediatric Society. He reported upon the work in Pennsylvania, and also upon the postgraduate courses which Dr. Paul W. Beaven is giving in Up-State New York. Delaware is gradually assuming more interest in the Academy. In Connecticut the program is well in hand with an active group of men. In New Jersey a state-wide health conference, called by the governor, is being participated in by the members of the Academy. The child health phase of this is largely directed by them.

In New York and the environs, Dr. Alexander T. Martin is taking an active interest in the work and did an especially good job with respect to the recent meeting. Dr. Henry E. Utter, in Rhode Island, is quite active. Dr. Thomas Foster, in Maine, has several projects in hand. In the Province of Quebec, Dr. Alton Goldbloom has interested several of the French Canadian pediatricians and three have been elected Fellows. This is working out quite well. Dr. Frederick F. Tisdall, from the Province of Ontario, is working on the question of voluntary health insurance for children. This work may be of great interest to the rest of the members of the Academy.

Dr. Julian M. Lyon of Ardmore, Pennsylvania, was recommended cochairman for Pennsylvania, to replace Dr. Joseph Stokes, Jr., resigned.

Region II.—Dr. E. C. Mitchell announced that the meeting of Region II would be held most likely the first week in January; in Florida or some place on the Gulf of Mexico.

The resignation of Dr. James W. Bruce as associate chairman of Region II was accepted. Dr. Hugh Leslie Moore of Dallas, Texas, was recommended for the appointment.

The resignation of Dr. Clark H. Hall of Oklahoma City, as state chairman of Oklahoma, was accepted and Dr. Carroll M. Pounders was recommended to replace him.

Dr. Arthur G. Jacobs of Memphis was recommended for cochairman of Tennessee.

It was voted that a committee be appointed to review and revise Articles V and VI of the Constitution with the idea of inclusion of an honorary fellowship; this to be referred to the Executive Board for action and submitted to the membership by the middle of October.

Region III.—It was decided that Region III would hold its next meeting in Kansas City probably the first week in May; the exact date is not yet determined.

Dr. Edgar E. Martmer of Detroit, was recommended for reappointment as associate chairman.

Dr. John C. S. Brown was recommended for chairman of the Province of Saskatchewan.

Dr. A. Graeme Mitchell submitted the motion presented by the State Chairmen of Region III:

"It was moved and carried that the question of enlarging upon the interpretation of the term 'crippled children' in the national program to include certain other seriously handicapped children, be brought to the attention of the Executive Board." The advisability of suggesting a plan to the Children's Bureau was also discussed.

It was moved and carried that the Executive Board is interested and would take up the matter with the Children's Bureau.

Dr. Mitchell also presented the motion carried by the state chairmen, "That the American Academy of Pediatrics devise such suitable ways as seem practical for informing the membership along those particular lines that have to do with the child, such as social, educational work, etc."

It was moved and carried that the matter be referred to the Committee on Cooperation with Nonmedical Groups and Societies with a suggestion that they inform the individual members of the Academy in the matter of technique and approach to lay groups, P. T. A., social agencies, etc., the Secretary to inform Dr. Lee Forrest Hill of the action taken by the Executive Board.

Another motion presented by Dr. Mitchell at the proposal of the state chairmen was discussed: "It was the consensus of opinion that the medical care of the child be directed by a qualified pediatrician while under orthopedic care, under the national crippled children's act; the pediatrician to be remunerated for such service."

It was decided that the term "qualified" should be taken up with the Children's Bureau suggesting that the physician should be certified by the American Board of Pediatrics where possible.

At this point, Dr. Stanley Nichols moved that a pediatric consultant should be appointed to each children's commission in this country. The motion was carried.

Region IV.—The next meeting of this region is to be held in Seattle in the spring of 1940.

The resignation of Dr. H. L. Moon of Seattle, as state chairman of Washington, was accepted, but his successor was not appointed because Dr. Edward B. Shaw requested some time to look into the matter.

Committees.—

The report of the Committee on Child Health Relations was accepted and approved.

The report of the Committee on Contact Infections was accepted and approved. The booklet submitted by this committee for approval was referred to Dr. Stanley Nichols. After conference with Dr. Fairfax Hall, the booklet is to be resubmitted to the Executive Board in November.

The report of the Committee on Nonmedical Groups and Societies was accepted and the recommendations of this committee approved. It was moved and carried that the booklet concerning the motion picture film be referred to the committee for publication.

It was decided that the Academy could not grant the request of the Committee on Medical Supervision of Camps to pay the expenses of that Committee to the Cincinnati meeting.

The report of the Committee on Hospitals and Dispensaries was accepted and approved.

The report of the Committee on Immunization Procedures was accepted and approved. The Secretary was authorized to have the report presented printed, the expense not to exceed $200.

The report of the Committee on Infantile Paralysis was accepted as read. It was the consensus of the Executive Board that a letter be written to the National

Committee on Infantile Paralysis urging them to have a qualified pediatrician in all state and county groups expending these funds.

The report of the Committee on Legislation was accepted and approved. The recommendation on the discussion of the Wagner Act was accepted and this committee was requested to make an analysis of the act as it relates to pediatrics and to present this analysis first to the Executive Board for approval the day before the meeting of the Academy in November and later at the business meeting of the Academy.

The report of the Committee on Medical Education was accepted and approved.

The report of the Committee on Mental Hygiene was accepted and approved.

The report of the Committee on Neonatal Morbidity and Mortality was accepted and approved. On recommendation of this committee it was decided to change the name to the Committee on Problems of the Fetus and the Newborn Infant.

The report of the Committtee on Nursing Education in Pediatrics was accepted as read.

The report of the Committee on Pediatric Awards was accepted as read.

The report of the Committee on Revision of the Pharmacopoeia was accepted. The first recommendation regarding the publication of articles by qualified pediatricians and investigators in the JOURNAL OF PEDIATRICS, was referred to the committee with the request that it communicate with the Editorial Board of the JOURNAL. The Executive Board did not approve the adoption of a loose-leaf compendium, nor the third recommendation for printed charts for the more common poisons and their antidotes. The fourth recommendation, regarding lead poisoning, met with sympathetic response on the part of the Executive Board and was referred to the committee with the request that this body should draw up such recommendations as would meet the situation and submit them to the Executive Board.

The report of the Committee on School Health and School Health Education was accepted and approved.

The report of the Council for Pediatric Research was accepted and approved.

The report of the Nominating Committee was as follows:

For vice-president (president-elect): Dr. Richard M. Smith, Boston, Mass.

For chairman of Region I: Dr. Stanley Nichols, Asbury Park, N. J.

The president was authorized to appoint a liaison committee to act with a like committee from the Section on Pediatrics of the American Medical Association.

A copy of "The Standards for Directories for Mother's Milk," submitted by Dr. Fritz B. Talbot, approved by the Committee on Hospitals and Dispensaries, was discussed and the Secretary was authorized to send this to the JOURNAL OF PEDIATRICS with the hope that it might be published there.

The request of Dr. James W. Bruce that we authorize and subsidize the publication of Round Tables and Panel Discussions as separate reprints from the JOURNAL OF PEDIATRICS, was not granted by the Executive Board, but it was suggested that Dr. Bruce be requested to take this matter up directly with the C. V. Mosby Company if he were interested.

The Treasurer was authorized to contribute $10 to the National Council for Mothers and Babies.

A letter from the Medical Library Association regarding the publication of an abstract journal was read. It was moved and carried that the Executive Board felt that, in view of the fact that the *American Journal of Diseases of Children* already took care of this need, it would be duplication of effort to cooperate in the sponsoring of such an abstract journal.

A letter from Dr. James J. Donahoe of East St. Louis, Ill., regarding medical protective insurance was read. It was decided that he be asked for further informa-

tion respecting this subject since the information which he gave in his letter did not conform to much of what the members of the Executive Board knew concerning the subject.

Dr. Sterling H. Ashmun of Region III brought up the subject of health insurance for dependents. It was decided that the president be empowered to appoint a Committee on Medical and Hospital Insurance for Children.

Report on Publicity

On January 1 of this year, we began a public educational program for the American Academy of Pediatrics that would accomplish two things: (1) increase the prestige of pediatricians with the public and the medical profession, and (2) enlist public and professional cooperation in the work done by the Academy in the child health field.

We proposed to bring this about by presenting the Academy, its aims, and objectives, to the millions of people who are daily readers of newspapers and magazines and listeners to radio programs. In the six months that have elapsed since this program was inaugurated, we have accumulated certain tangible results to report at this time to the Executive Board of the Academy.

I have here an outline map of the United States. Every star and dot on this map represents a city where one or more stories concerning the Academy have appeared. The gold stars mark cities where from three to thirty-one stories were used (San Francisco newspapers alone have carried thirty-one Academy stories), while the red dots are used for cities where one or two stories were published.

In total, we have mounted 443 clippings from newspapers dealing with material released by us. I would like particularly to call your attention to the eleven editorials that are numbered among these clippings. A newspaper editor never assigns any topic to his editorial department unless he feels it to be of vital interest to the public. He reserves judgment about an association and its work until he is personally sold on its importance. Nine of these eleven editorials on the Academy have reached our office in the past week and every mail is bringing more of them in. Represented among newspapers that are editorializing child health, as interpreted by the American Academy of Pediatrics, are the *St. Louis Post-Dispatch*, the Washington, D. C., *Post*, the Columbus, Ohio, *State Journal*, and the *Philadelphia Public Ledger*.

In addition to these 443 newspaper stories and editorials, three magazines with a total national circulation of 4,101,658 readers have printed stories about the Academy. The three magazines are *Time Magazine, Newsweek* and the *Woman's Home Companion*.

These newspaper and magazine clippings are bound in seven books which I shall leave with you to be reviewed at leisure. Three Academy events made the news basis of the clippings: the beginning of a contact infections drive in Westchester County, N. Y., the annual meeting of Region IV in Oakland, Calif., and the annual meeting of Region I in New York City.

Through our efforts, four New York City radio stations (WHN, WOV, WINS and WMCA) broadcasted Academy programs during the meeting of Region I.

Much of our time during these past six months has been used in laying the foundation for future publicity. (We have found it to be true of all our accounts that at least six months of background work has to be done to get an education program under way.) In the case of the American Academy of Pediatrics, we have placed great emphasis on personal contacts with editors and writers on child health subjects for the purpose of familiarizing them with the activities and scope of the Academy.

I personally have visited the editors of all the women's and general magazines to acquaint them with the Academy, and a series of letters has been sent to key

newspaper editors, editorial writers, and writers of syndicated articles dealing with child welfare throughout the country.

On January 17, we arranged an "informational" luncheon at the Waldorf-Astoria Hotel, in New York, which was attended by 11 editors and writers representing publications of national importance. Among the guests at the luncheon were: Bruce Gould, editor of the *Ladies' Home Journal*, Mrs. Clara Savage Littledale, editor of *Parents' Magazine*, Miss Katherine Bourne, associate editor of *Cosmopolitan Magazine*, Miss Katharine Clayberger, associate editor of *Woman's Home Companion*, Miss Camille Davied, homemaking editor of *McCall's* magazine, Miss Aimee Larkin, associate editor of *Collier's Magazine*, and Mrs. Eunice Barnard of the Alfred P. Sloan Foundation.

Sessions of the Region I meeting held recently in New York were attended, at our invitation, by most of these editors and Dr. Walter H. Eddy of *Good Housekeeping Magazine*, Howard Blakeslee, science editor of the Associated Press, and Mrs. Gladys Huntington Bevans, whose child care and training articles are syndicated to hundreds of newspapers in all parts of the country.

Since the editorial contents of most magazines are prepared from four to six months in advance, our work in this field is just beginning to bear fruit. The May issue of *Woman's Home Companion* (which has a circulation well over 3,000,000) made an editorial on the Academy's contact infections campaign the lead editorial for that issue. Material for a similar editorial has been requested by the *Ladies' Home Journal*, and several other leading women's magazines have indicated their intentions of assigning stories concerning child health and the Academy to staff writers in the near future. Accounts of the New York regional meeting headed the sections devoted to medicine in both *Time* magazine and *Newsweek* for June 12.

To be completely effective, our program should take cognizance of the local activities of Academy committees, as well as issues of national interest and importance. We feel that we have made great strides in this six-month period in putting the Academy before the nation as a whole and that a creditable start has been made in assisting members with local publicity problems.

At the beginning of our work, we wrote 16 pediatricians in various parts of the country, whose names had been given us by Dr. Fairfax Hall as having reported local progress with the contact infections campaign. We asked these doctors to keep us informed of their plans and to send us advance copies of any addresses to be made by Academy members in their locality. Over half of the pediatricians complied with our requests, and we were able to make local publicity suggestions to them.

In North Carolina, we released two reports made by Dr. Wilbert C. Davison on infant mortality and diphtheria immunity in Durham to the newspapers of that city.

In Illinois, we have worked with the Academy's state committees on school health, preventive pediatries, and mental hygiene to plan an effective publicity schedule for releasing the findings of these committees.

As more members become aware of our function as Department of Public and Press Relations of the Academy, we can increase our helpfulness in local publicity problems.

At the conclusion of our first six months as representatives of the Academy, over 35,000,000 people have read stories in their newspapers and magazines about the American Academy of Pediatries and its theories of child protection and care. A radio audience of approximately 2,000,000 listeners have heard members of the Academy speak on subjects vital to child health. More important still, the editors of the country know what the American Academy of Pediatrics is and what it stands for.

Respectfully submitted,

LAWRENCE H. SELZ.

Report of the Chairman of the Child Health Relations Committee

Following the adoption by the Executive Board in November, 1938, of the Child Health Relations program recommended at the meeting of that committee in June, 1938, in California, the state chairmen have been requested by the president of the Academy to appoint Committees on Child Health Relations in each state to forward this program.

These committees have been appointed in forty states and the program of the committee and a draft of sound foundations for child health programs sent to the chairmen of committees requesting an outline of activities desired.

In view of the fact that certain items in paragraphs 4 and 5 of the program adopted in November proved to have several statements which conflicted with the established policies of the Children's Bureau, its relations to the State and Territorial Health Officers Association cited in paragraph 5, a complete circularization to all states has been deferred pending a meeting to adjust the program, if possible, so that it might enlist the entire support of the medical staff of the Children's Bureau before presenting the activities of the program.

The chairman of the committee met the assistant-chief and director of the medical staff of the Children's Bureau, Dr. Martha Eliot, and also Dr. Bierman, Dr. Hood and Dr. Murray of the staff, at the regional meeting in New York City on June 1, 1939, and with the assistance of President Helmholz and Secretary Grulee of the Academy, adjusted the program to the agreement of all present. This program, together with the sound foundation for any child health program, is hereby submitted to the Executive Board for their approval, and if so approved, will be then submitted by mail to the members of the Child Health Relations Committee. When so adopted, this program will be mimeographed and sent to all state chairmen of Child Health Relations Committees, with continued effort to have each state vigorously attempt, within the coming year, to carry into effect in each state as much as possible of this most important administrative policy.

In direct proportion to the success in any given state in the carrying out of this policy, the American Academy of Pediatrics will become the permanent key group in the promotion of child health activities, which is a most proper position for the Academy to assume.

Modified Child Health Relations Program

We recommend that:

1. The various state chairmen with the Fellows in their states devise some feasible method for assuming leadership of the child health policies in the respective state medical societies. (It is suggested that, where necessary, effort be made to establish in each state medical society a committee on child health with adequate representation of Academy members.)

2. At the request of any state chairman, the president of the American Academy of Pediatrics address a letter to the president of the state medical society, enclosing a list of the Academy Fellowship of that state and pointing out the value of utilizing the Fellows as leaders in all types of child health activities in that state.

3. On the basis of information submitted by the state chairmen, the president of the Academy write to the directors, or commissioners, of their state boards of health, and other state public officials having to do with any phase of child health, volunteering the assistance of the Academy Fellowship in carrying out the child health phases of the state health program.

4. The president of the American Academy of Pediatrics urge the conference of state and provincial health authorities to adopt a policy whereby (1) the

state fellowship of the Academy and the child health committee of each state medical society act as a part of the advisory group on all child health activities and (2) these two groups jointly endeavor to coordinate the child health activities of the state departments of health and the state medical societies in each state.

5. Each state chairman of the Academy recommend that (1) Fellows or other suitably qualified physicians act as child health advisors to all official and nonofficial agencies in the state having some phase of child health activities in their program and (2) such qualified physicians be appointed to governing bodies of such agencies.

6. It is the sense of this Committee that the American Academy of Pediatrics use its influence to promote, through joint action of its State Child Health Relations Committee and the child health committees of the state medical societies, the establishment and maintenance of desirable standards regarding qualifications of all official personnel in health departments, and to work for the adoption of merit systems in all states and their political subdivisions in accordance with standards established by national organizations in their respective fields

By the above methods each state Fellowship of the American Academy can act as the responsible coordinating group for the state departments of health and other official state agencies, the state medical societies and the lay agencies having child health programs for the definite development of better child health activities in each state.

The Essential Three Groups Necessary for Permanent Sound Foundation for Any Child Health Program

Group 1.—Service Group—Pediatricians (plus full-time health service professionals).

Physicians
Dentists
Nurses
Hospitals
Pharmacists

Functions of Group 1: To study child health needs, and prepare as a group to cooperate with administrative and promotion groups in child health activities laid first by the service group and the administrative group.

Group 2.—Administration Group—Health officials and other public officials having to do with any type of child health activity.

Functions of Groups 1 and 2: To develop health programs.

Group 3.—Promotion Group—Lay child health agencies and other health and welfare agencies interested in some phase of child health.

Functions of this group: Where necessary, to stimulate Groups 1 and 2 into needed child health activities.

Promotion
Publicity
Raising of private funds
Health education as to health plans laid first by the service group and the administration group.

Respectfully submitted,
STANLEY NICHOLS.

Report of the Committee on Contact Infections

Academy membership has been circularized with reprints of "The Real Servant Problem" and "Healthy Workers in the Home." A leaflet, "For the Sake of the Children," was prepared for distribution to patients through the offices of physicians. This was printed by Mead Johnson & Company, and over 100,000 have been taken by members of the Academy.

A meeting was held in New York City, by arrangement of Mr. Lawrence H. Selz, at which the objectives of this Committee were discussed freely with editors of eight leading national magazines, Associated Press and United Press representatives. The result has been publication of several magazine and newspaper articles and editorials dealing with the subject of preventing infection of children by adults.

State committees on contact infections have been appointed in 42 states, also Washington, D. C., and Hawaii. Many of these committees have taken active steps to promote periodic health examination of adults in contact with children. Others are endeavoring to bring about the acceptance of this principle by county medical societies. Many of the state committees are yet incompletely organized. Some are giving their attention to other matters than that for which they were appointed.

Dr. Oliver W. Hill reports that in 1938, in Knoxville, Tenn., among domestics, 571 persons with syphilis, 67 persons with active tuberculosis, and 5 typhoid carriers were picked up and put out of circulation.

A compilation of all pertinent facts and statistics regarding contact infections is being made by the Committee in order that it may be passed on to the state chairmen as material for publicity and educational purposes.

The outlook for progress is encouraging, but much remains to be done before the program is completely in effect.

Suggestions for the Continued Activities of This Committee

1. Keep in touch with the state committees to correlate and assist their activities.
2. Promote publicity in the medical and lay press in order to acquaint the medical profession and public with the need for protecting the child from infected adults.
3. Contact national health organizations, health departments and departments of education in order to secure cooperation in this health movement.
4. Take steps to bring about examination of school teachers in order to remove from teaching all who have infectious tuberculosis.
5. Continue to encourage arrangements for adequate periodic health examination of domestic servants who care for children.
6. Encourage periodic examination of parents and other members of the family.
7. Ask pediatricians to have examinations themselves because of their association with children and in order to set an example to the families of their patients.

Respectfully submitted,
FAIRFAX HALL, Chairman
GAYLORD W. GRAVES
REGINALD HIGGONS
OLIVER W. HILL

Report of the Committee on Cooperation With Nonmedical Groups and Societies

The report of this Committee at this time may be rather brief since a detailed outline of its proposed activities was presented to the Executive Board last November. The Committee has pursued its cooperative efforts with the Summer Round-Up Division of the National Parent-Teachers Congress along the lines indicated in the November report. In response to a request from the secretary, subcommittees to work with our national committee have been appointed in every state in the country.

Dr. Lillian R. Smith, national chairman of the Summer Round-Up, addressed a letter to each of her state chairmen, a copy of which is appended to this report, in which it was suggested that the lay officials contact the Academy subcommittees. Thus, a workable means has been provided in each state to bring the two groups together.

Chairmen of these local subcommittees have received two enclosures, each of which set forth the main objectives of the national committee. Copies of these enclosures are also appended to this report.

Essentially, the recommendations made to the subcommittees were that:

1. The local subcommittee receive official recognition from its state medical society.
2. That the local subcommittee, when contacted by Summer Round-Up officials, lend every possible assistance, subject to local conditions, in an effort to further the Summer Round-Up movement.
3. The local subcommittees, through the medical and lay press, by radio, and by talks before county and state medical societies and other groups, present the essentials in a periodic health examination of a child.

No definite opinion can be given at this time regarding the extent of activities in the various states. However, from personal contact and conversation with various men at the meeting of the American Medical Association in St. Louis, the chairman is inclined to believe that Academy members in general are in agreement that the cooperative project is a sound one and that over a period of years a good deal can be accomplished in educating both parents and physicians to the benefits to be derived from more careful health examinations in children.

Dr. A. B. Schwartz, chairman of the Wisconsin group, reports, "In order to provide a better common understanding of what periodic examinations should entail, we have introduced as one of the features of our next state medical society meeting a 25-minute symposium on the subject. Five men, representing the fields of pediatrics, orthopedics, ophthalmology, and otolaryngology, will each spend five minutes on the details of practical examination. Put together, the material should give us a good practical working brief on the subject. What we are able to do with it after we get it, only time can tell.

"I am convinced that your committee's conclusion as stated in your letter of last January is correct and that the problem is in the main one of educating the general practitioner to the importance of routine examinations thoroughly done."

The Committee expresses its hope that many more states will undertake a similar program to the one planned for Wisconsin.

The production of the sound moving picture film depicting the essentials of a periodical health examination is well under way under the direction of Dr. Arthur H. Parmelee of Chicago and of Mead Johnson & Company. It is expected that the film will be ready sometime in the fall. The committee is looking forward with a great deal of enthusiasm to the completion of this picture for they believe it will find a wide range of usefulness.

The one recommendation the Committee would make to the Board at this time is that it consider the matter of preparation of a pamphlet based upon the film, detailing Academy standards in a health appraisal of a normal child. Among other things, such a pamphlet ought to discuss the differentiation of functional heart from organic murmurs; the method of using an E or Snellen chart for determining gross abnormalities in vision; a simple method for determining hearing defects in both high and low notes (whispered and spoken voice); and, finally, something about posture defects including flatfeet. Such pamphlets distributed to physicians who view the moving picture film should be of considerable usefulness to them subsequently. The Committee would recommend that the Board designate some repre-

sentative or representatives of the Academy to prepare such a pamphlet and that when the pamphlet is completed, it bear some title such as, "Prepared by the American Academy of Pediatrics."

Respectfully submitted,

LEE FORREST HILL, Chairman
DENNIS H. KELLY, Secretary
C. A. ALDRICH
JAMES W. BRUCE
JOSEPH A. JOHNSTON
ALBERT D. KAISER
MARGARET NICHOLSON
WARREN SISSON
HENRY E. UTTER

Report of the Committee on Hospitals and Dispensaries

All the data for the report on means of avoidance of contact infections in children's hospitals have been collected. The secretary is preparing a report at the present time, and we expect it to be completed in the near future. This report is being compiled from material gathered by the questionnaire method from all children's hospitals in the United States and Canada. At the present time the Committee has no particular recommendations to make.

Respectfully submitted,
GEORGE F. MUNNS, Chairman

Report of the Committee on Infantile Paralysis

The Committee has held no meeting because there has been no particular reason for one. The chairman has been in touch from time to time with the National Committee for Infantile Paralysis. It is possible that there may be a function for this Committee some time in the future, and it is suggested, therefore, that it might be continued in spite of its present inactivity.

Respectfully submitted,
A. GRAEME MITCHELL, Chairman

Report of the Committee on Legislation

The Committee on Legislation now has under consideration Senate Bill 1620, known as the "National Health Act of 1939," introduced in the Senate on February 28, 1939, by Senator Wagner of New York.

This bill is now being considered by the Senate Committee on Education and Labor, which is conducting hearings from time to time.

Title V, relating to maternal and child health services, is of special interest to the members of the Academy, and the remaining portions of the bill are of concern to physicians in general.

Because of the importance of this proposed legislation as it may affect members of the Academy, request has been made to the Executive Secretary that this subject be included in the agenda on the occasion of the annual meeting of the Academy in Cincinnati, Nov. 16-18, 1939.

Respectfully submitted,

JOSEPH S. WALL, Chairman
ISAAC A. ABT
J. I. DURAND
PHILIP VAN INGEN
ALFRED A. WALKER

Report of the Committee on Mental Hygiene

The Committee on Mental Hygiene has been active in carrying out the program which was submitted last year and approved by the Academy. The most important projects of that program are:

1. The teaching of mental hygiene in the pediatric departments of medical schools. Medical schools generally have failed to provide adequate training in

mental growth and development and in mental hygiene problems of children. The Committee feels that this training is best given in the pediatric departments. The Chairman of the Educational Committee of the National Committee for Mental Hygiene suggests a minimum of 12 hours.

2. Adequate training of pediatric interns and residents. Training centers for physicians who plan to limit their practice to pediatrics generally do not have facilities for training and experience in the problems of mental hygiene. It is felt that experience in a mental hygiene clinic, preferably in the hospital and clinic in which the intern is studying, is necessary in order to enable him to treat the child as a whole.

The Committee on Mental Hygiene again recommends that the Academy as a whole undertake to stimulate interest in these two projects.

3. In order to stimulate a more active interest in mental hygiene among pediatricians and to bring to their attention the valuable information found in medical literature, other than pediatric journals, a series of articles dealing with pertinent facts on mental health are being prepared by outstanding writers for publication in the JOURNAL OF PEDIATRICS.

The Committee welcomes suggestions from all members of the Academy and feels that the support and cooperation of all members is essential to the successful carrying out of the above program.

Respectfully submitted,

BERT I. BEVERLY, Chairman	BRONSON CROTHERS
C. A. ALDRICH	GEORGE MOHR
FREDERICK H. ALLEN	ARTHUR H. PARMELEE
HORTON CASPARIS	VICTOR E. STORK

Report by the Chairman of the Committee on Neonatal Morbidity and Mortality

Your Committee has been active during the year in conjunction with a similar committee of the American Pediatric Society. Members of these two committees have held several conferences to consider the problems which call for solution in this field and the ways in which the Committee might act to promote certain desired objectives. Your chairman has also corresponded with many interested persons not members of the Committee. It has been recognized that no substantial progress could be made in dealing with problems of the newborn without the active cooperation of obstetricians. Dr. Dunham and your chairman had a conference with Dr. Adair in Chicago last November in the hope of securing the cooperation of the American Committee on Maternal Welfare. The latter includes among its members representatives of the principal obstetrical societies. Dr. Adair agreed to appoint a subcommittee of the American Committee on Maternal Welfare to cooperate with the pediatric committees on neonatal morbidity and mortality. The appointments were as follows: Dr. Philip Williams, Philadelphia; Dr. Robert De Normandie, Boston; and Dr. Fred Adair, Chicago.

A joint meeting of these committees was held in New York City on April 2 and was attended by the following members:

Fred Adair, Chicago Philip Williams, Philadelphia	Representing the American Committee on Maternal Welfare
Ethel Dunham, Washington Warren Sisson, Boston Rustin McIntosh, New York	Representing the American Pediatric Society
Harold Stuart, Boston Stewart Clifford, Boston	Representing the American Academy of Pediatrics

Members absent were: Robert De Normandie, Boston (American Committee on Maternal Welfare); Julius Hess, Chicago (American Pediatric Society); and Laurence De Buys, New Orleans (American Academy of Pediatrics).

At this meeting a joint committee was organized under the chairmanship of Dr. Adair, and with Dr. Williams and Dr. Stuart as vice-chairmen representing obstetrics and pediatrics, respectively. These officers, together with a secretary to be appointed by the Executive Committee, were empowered to act as an Executive Committee. It was agreed that, if funds could be secured, the secretary should be chosen on the basis of opportunity to travel and give time to the Committee and should receive remuneration.

In order to extend the influence of the activities of this joint committee, it was felt that it should directly represent the American Gynecological Society and the American Association of Obstetricians and Gynecologists. These societies are already represented indirectly through the American Committee, but they will be asked at forthcoming meetings to confirm these appointments or add direct representatives. The suggestion was also made that the Obstetric and Pediatric Sections of the American Medical Association might be asked to appoint one or more representatives. The Pediatric Section has since appointed Dr. Arthur H. Parmelee of Chicago and Dr. W. C. C. Cole of Detroit to be its representatives. The American Pediatric Society has also reappointed three of its five previous representatives, Drs. Sisson, Dunham, and Stuart.

In order to make the name of the Committee sufficiently comprehensive, it was proposed that it be changed to the "Joint Committee of Obstetric and Pediatric Societies on Problems of the Fetus and the Newborn Infant."

Owing to the desire to keep the membership of the joint committee small, to promote efficiency, and to have more nearly equal representation of obstetricians and pediatricians, it was proposed that the membership of the committees representing single societies should not exceed three in number.

The joint committee finds ample evidence that fetal and neonatal morbidity and mortality could be materially reduced through a more widespread application of present knowledge. It believes that the Societies represented and those that may be included could promote interest in bringing about improvement along certain clearly indicated lines. The Committee, therefore, proposes to make a careful study of one or more aspects of this broad problem during the coming year and to submit concrete recommendations, which it hopes the members of the Societies represented will sponsor in their respective communities. In subsequent years, other problems may be taken up for intensive study and report.

Proposals will take into account the needs and facilities of the country as a whole and be suitable as far as possible for general application. They will be concerned with the activities of practicing physicians, hospitals, and public health organizations. An attempt will be made in preparing each report to define the problems in the field under consideration, to discover the fundamental needs for prevention or correction, and to recommend ways and means of meeting these needs under varying circumstances. The general subjects to which it is proposed that attention be directed are the following:

1. Standard definitions of terms.
2. Revisions in the nomenclature of causes of death and in the list of acceptable diagnoses.
3. Adoption of new stillbirth, birth, and death certificates, and recommendations as to their use.

4. Need for more frequent and careful autopsies on stillbirths and neonatal deaths, and recommendations as to procedure.
5. Hospital records and medical routines (physical examination of newborn infants, etc.). Hospital statistics, analyses of records, staff conferences.
6. Community studies of neonatal morbidity and mortality. Reports and analyses—follow-up studies.
7. Hospital regulations and licensure.
8. Requirements for protection of neonates at different periods and under varying circumstances. Standards for facilities and care.
9. Means of securing widespread attention to recommendations.

Considerable progress has already been made in collecting material and in arriving at agreements as to recommendations which should be made under a number of these headings. For example, Dr. Williams has been working on a plan for the analysis of stillbirths and neonatal deaths, and has submitted forms for the collection of data. Your Committee is not prepared, however, to submit recommendations at this time dealing with any of the subjects listed above.

Lack of funds has been recognized as a real handicap to the accomplishment of the proposed program. The Executive Committee must be in a position to meet from time to time, and the full committee should be able to have at least one unhurried conference each year. The American Academy of Pediatrics made $150 available to the chairman for expenses incurred in connection with meetings this year. About half of this sum has been spent to date, an itemized account of which has already been submitted. The chairman will require an allowance to carry on the activities of the Committee during the coming year. A means of financing a meeting of the full joint committee next fall has been afforded by the Children's Bureau. Its medical director has offered to pay the traveling expenses of all members for the purpose of attending such a conference in Washington and to be host to the conference there. The joint committee acted favorably on this offer and set a tentative date for such a conference next December. Your Committee requests that the Society authorize acceptance of this offer of the Children's Bureau. It is possible that the Bureau may extend this offer to include the services of a secretary for a period preliminary to and following this conference.

The joint committee authorized its Executive Committee to seek a grant to cover the estimated needs of the Committee for a three- or five-year period. The amount requested would be sufficient to cover the expenses of attendance upon meetings, the part-time services and travel of a medical secretary, and stenographic assistance. It is not proposed to act upon this authorization until after the proposed conference in the fall, when it is hoped that a more specific program be in hand.

Recommendations:

1. The present Committee on Neonatal Morbidity and Mortality be reappointed but the name of the Committee be changed to "Committee on Problems of the Fetus and the Newborn Infant."
2. This Committee be authorized to join with similar committees representing pediatric and obstetrical societies, working through the newly formed joint committee of similar name.
3. This Committee be authorized to accept the offer of the Children's Bureau to finance a meeting of the joint committee in Washington next fall and to participate in this meeting.

4. The American Academy assign $150 to meet the expenses of its chairman during the coming year in attending meetings of the Executive Committee of the joint committee and for other expenses of the Academy committee not covered by the offer of the Children's Bureau.

Respectfully submitted,

HAROLD C. STUART, Chairman
STEWART CLIFFORD
LAURENCE DE BUYS

Report of the Committee on Nursing Education in Pediatrics

The Academy Committee on Nursing Education in Pediatrics has cooperated with two committees of the National League of Nursing Education. These two committees are the Committee on Nursing Education and the Subcommittee for the Study of Advanced Courses in Pediatric Nursing. Miss Corinne Bancroft, Director of Nursing Education in the Children's Hospital, Cincinnati, is chairman of the subcommittee. The cooperation has also been welcomed by Miss Ahlfield J. Axelson, who is acting chairman of the Committee on the Child, National League of Nursing Education.

The Academy Committee, in association with Miss Bancroft, has outlined certain courses in advanced pediatric nursing and in advanced clinical pediatric nursing; both of these have been used in the Children's Hospital of Cincinnati during the past year, and courses have apparently been satisfactorily received and have seemed to be practical.

It is the recommendation of this Committee that it continue this type of cooperation and follow the progress made by the committees of the League of Nursing Education. The members of these committees represent several schools throughout the country which are particularly interested in postgraduate courses in pediatric nursing.

Your Committee hopes to be able to present the plans for these courses to the Academy at its next report.

Respectfully submitted,

MERLIN L. COOPER, Chairman

Report of the Committee on Revision of the Pharmacopoeia

This report will discuss briefly the following items of work that have been either carried out or taken under consideration during this past year, namely:

1. Representation (membership) on the revision of the United States Pharmacopoeia and National Formulary.

2. Publication of authoritative articles designed to inform the medical profession at large and the pediatric specialty in particular of the latest trends and developments in the management and therapeusis of children's ailments.

3. Publication of a loose-leaf compendium containing notation of all the remedial agents of pediatric usefulness and necessity (a) which may serve the pediatrist and internist as a guide, in concise form with posologic scales as to the use of standard official and approved unofficial remedies (b) and which may also serve in the instruction of undergraduate and graduate students in the essentials of pediatric therapeutics.

4. Participation in a campaign to reduce by the dissemination of proper information as to their causes and management, poisoning and death from poisoning; particularly poisoning from unwarranted use of lead paints, and these as they are employed especially upon infants' toys and furniture.

Representation (Membership) on the Revision of the U.S.P. and N.F., 1940.—The committee appointed to represent the American Academy of Pediatrics as to revision of the U.S.P. and N.F. has not held a formal meeting since last year. However, applications have been filed with the officers of the U.S.P. and N.F. for pediatric representation on those bodies. It is hoped that membership will be granted to us, and that both groups working together will be able to improve the present standards of both texts regarded from the pediatrist's point of view. Our application has been motivated by the conviction that the general practitioner should no more be expected to designate remedial agents for the use of infants and children than the pediatrician should be asked concerning those same remedies for use by adults. Moreover, the phenomenal development of the pediatrist's specialty in recent years with the accompanying adoption of newer remedies as these have found their way into the practice of the specialty has made necessary a careful, scrutinizing survey of these agents in order that each may be evaluated upon its sure merit. Naturally, it is to be insisted that the examination and evaluation of these newer agents must come from those most peculiarly qualified to judge their efficiencies. The excellent organization of the Academy can render most worthwhile service to the officers of the U.S.P. and N.F. by presenting individual and collective opinions upon the remedies considered for their acceptance.

Publication of Articles by Qualified Pediatricians and Investigators in the Journal of Pediatrics.—A plan for such articles and their publication by this body, as already suggested to the Executive Committee, has enjoyed enthusiastic comment. Once again we would refer the Executive Committee to the series of special articles that recently appeared in the *Journal of the American Medical Association*. The excellent articles there were the result of suggestions made by several members of the Pharmacopoeial Committee of Pediatrics to the Chairman of the U.S.P. They specifically illustrate what can be done in rendering a really useful service in the field of pediatrics.

The Adoption of a Loose-Leaf Compendium Covering Official and Nonofficial Remedial Agents of Therapeutic Usefulness and Necessity in Pediatrics.—Since the Executive Committee of the Academy has declined to give its endorsement to a proposal for a text to be entitled "Pediatric Therapeutics and Formulary" broached in an earlier report to the Academy, it is now proposed that a ready reference manual of practical pediatrics and useful procedures be considered for compilation and publication, preferably, if regarded as a feasible project, in a loose-leaf arrangement.

A compendium of this type would serve as a help to physicians in practice, as a practical guide for routine hospital dispensary and ward work, and as an aid in the instruction of undergraduate and graduate students in the essentials of pediatric therapeutics. It should include such agents, both official and unofficial, as a Committee would accept. Thus it would acquaint the profession with new therapeutic remedies as they find their way into pediatrics as well as present the standard therapeutic agents long in use, with, wherever possible, their proprietary equivalents. In each instance, a brief chemical description would be provided, together with the therapeutic indication and a suggested method of administration. The chairman and his committee would make it their business to solicit the best authorities for assistance in securing the necessary information. Lastly, the information secured and properly drawn up would be subject to review in all its items by the Chairman and his Committee before any final acceptance was made. Further, as a concluding step in the approval of proper remedial agents, it might be well to desig-

nate each chemical agent or drug "A.A.P.C.," having the endorsement of the Academy Pharmacopoeial Committee. Thereafter, from time to time, preparations would be added to, or deleted from, the text in accord with the trend in advancing therapeutics. Thus the Committee while functioning independently of the U.S.P. would be capable of working as an integral part of it.

It is further suggested that if the proposed manual be approved, the size be kept small, with a page not larger than 6 by 9 inches. It must be repeated that the Committee feels that the profession would respond most favorably to the offer of such a compendium, and that probably a reputable publishing house would be willing to carry the publication at a rate that would not tax the treasury of the Academy.

An Attempt to Reduce Further Infant Morbidity and Mortality Caused by Lead Intoxication.—It is felt that a cooperative effort in company with the U.S.P. Committee should be made to eliminate the danger of lead poisoning to children as now often happens through the use by manufacturers of lead paint upon furniture, toys, and other articles intended for child consumption. Very definitely manufacturers should be made aware of the danger of lead intoxication to their customers of baby age from lead paint. Particularly is such an effort justifiable in view of the fact that there is now existing no valid and sufficient reason why vegetable paints should not be universally employed by manufacturers upon such goods.

Beyond this particular suggestion, however, this Committee believes and wishes to express its belief that its function should not be restricted to the adoption merely of official and nonofficial therapeutic agents. It should go farther and suggest the proper labeling of all remedial agents for the home, whether for internal medication or household use, and such other appropriate restrictions as might restrict thoughtless and careless handling.

The Committee also takes this opportunity to point out that toxicology as applicable to infants and children represents a much neglected phase of pediatric teaching. With the exception of one or two institutions, instruction in the toxicology of infants and children is not being given at all, the faculties of the colleges relying upon the general instruction of the departments of chemistry and toxicology to impart such knowledge, with the result that medical graduates bring little competence to the management of poisonings so far as they are incidental to children. Accordingly it is suggested that a list of the more common poisons and their antidotes be prepared for publication in placard form. These placards should then be made available to all accident and emergency hospital clinics, dispensaries, camps, etc. It is not improbable that some philanthropic firm, sympathetic to this good cause, might make possible by a donation the publication and distribution of the charts.

Recommendations.—The Committee recommends that:

(1) Provision be made for the publication of occasional articles under the caption "Pediatric Therapeutics," such articles to be published in the JOURNAL OF PEDIATRICS. The exact subjects and scope of each article should be determined by the chairman of this Committee. It is suggested further that these articles be prepared in each instance from the point of view of modern, progressive pediatrics.

(2) Consideration and approval be given to the proposal for a loose-leaf compendium, and that the Committee be requested to draw up detailed plans for its preparation.

(3) Consideration and approval be given to the proposal for a chart placard listing the more common poisons and their antidotes, to be distributed in those places where such a chart might be of immediate service.

(4) Consideration be given to the discovery of the most practicable means for reducing lead poisoning in children resulting from lead paint upon furniture, toys;

and that plans be formulated for cooperative effort with the manufacturers of children's furniture, toys and other articles, looking toward the elimination of such hazards to child life.

Respectfully submitted,

ISAAC A. ABT, Chairman
WILLIAM N. BRADLEY
BERNARD FANTUS
H. H. PERLMAN
LOUIS W. SAUER

Report of the Committee on School Health and School Health Education

The recommendation of the Executive Board that state committees be organized and attempt to carry out some one activity in the interest of school health programs has resulted in the organization of 38 state committees. This is indeed a recognition of the challenge which school health programs offer to the medical profession and is a very important step toward overcoming the neglect of this phase of public health which has been so general among medical leaders for many years.

It is impossible at this time to know what all the state committees are doing to carry out their objectives. The national committee has sent suggestions to all the state committeemen, two reprints on qualifications of personnel and an extensive report, "Suggested School Health Policies," prepared by the Committee on School Health of the American Public Health Association. Our suggestions have emphasized the importance of study of local problems and an investigation of what other interested groups have done and are working on at present in each state, particularly because of the great difference in state problems.

While it is obvious that the volunteer efforts of busy pediatricians in every state are being focused upon very complex and extensive problems, and in many places the policies and trends have become fixed by long tradition and medical neglect, there is already evidence that pediatric influence will be helpful in re-establishing medical leadership and guidance. State committees have reported special surveys in several states, in some states comprehensive survey reports are available from other sources. In several states the committees are working effectively with the state departments of health and education. In one state we shall send "Suggested School Health Policies" to 24 county school superintendents, selected as leaders through the cooperation of the state education department. One state has indicated that combined efforts of several groups working with our state committee have laid the groundwork for a wide support of a change in the mandatory annual medical examination law. Such a change is recommended in the interest of higher medical standards and to avoid the attempt to examine children too rapidly without time given to education regarding medical needs.

Recommendations.—As already indicated, specific recommendations on a national scale for extending the influence of the pediatric committees are not practical, but some further generalization might be suggested.

In most states there are pediatricians working in the schools, public health officials, university professors of hygiene and public health, and other educators who have studied the state school health problems and are aware of the more serious handicaps to progress on a statewide scale. Discussion and planning with these other state leaders should reveal "the one activity which should be emphasized first in the carrying out of this vast project."

Pediatric committees should be able to gain very readily the active support of organized medicine for those aspects of the school health program that are generally recognized by physicians as fields of health education which are appropriate and needed in the public schools. Such support and leadership will invariably lead to an understanding by educators of the high value of medical guidance in public education. To win appreciation of the need for medical advice is the first step necessary toward stopping any unsound trend in policy or procedure in the schools.

Trained health educators have been employed in several states at very little cost in proportion to the extensive influence they have exerted toward improving health teaching in the classroom. Recently several state departments of health have employed such health educators to work with teachers, principals, and school superintendents. Pediatric leaders in several cities have been the first to point out to the educators that health teaching could be improved by well-trained health education supervisors.

Pediatric disapproval of substandard medical judgments offered in schools and unsatisfactory advice given regarding the need for medical care should lead to a widespread medical support for correcting the attempt to offer more medical examinations than can be delivered. Emphasis upon quality rather than quantity should avoid the misunderstanding that the medical profession desires to limit the service. Study of the school services, no doubt, should lead to medical influence toward legislative changes in many states where mandatory annual medical examination laws interfere with sound medical guidance.

Another problem which is appreciated by the medical profession and which the educational administrators often neglect is the emphasis in the school upon perfect attendance. Rewards and honors given to classes for perfect attendance have a strong tendency to influence children to come to school when they should stay home in bed. The desire to maintain an attendance record readily influences the attitudes of children so that they come to school in the early stages of communicable disease or with illness that is aggravated by the stress and strain of the school program. In those states where state subsidies are based upon the attendance record instead of upon the number of pupils registered, there is often an excessive emphasis upon perfect attendance unless physicians and health officials have been effective in influencing the school authorities to recognize the problem.

As most physicians recognize this problem as one which requires medical advice to the school authorities, it is a project which can readily bring the support of organized medicine for a change in school health policies. State medical society support for the improvement of school health policies should strengthen the influence of pediatric leadership and so this problem may be particularly appropriate as a beginning step toward developing an advisory relationship with those who are responsible for the school health program.

Respectfully yours,

HAROLD H. MITCHELL, Chairman
ROCKWELL M. KEMPTON
M. HINES ROBERTS
A. CLEMENT SILVERMAN
CLIFFORD D. SWEET
ARTHUR E. WADE
ESTELLA F. WARNER
LEROY A. WILKES

Report of the Council for Pediatric Research

The Council for Pediatric Research completed, on May 1, 1939, the two-year experimental period contemplated in the grant from the Carnegie Corporation. The earlier experiences of the Council have been covered in previous reports, the last of which was presented in December, 1938. Since that time the progress of the Council has been rather encouraging so far as the receipt of definite grants for

research to be allocated through our agency are concerned. During the winter and spring seasons we have received grants totalling $19,735, in addition to fees to the Council amounting to $2,500. The clinics to which these grants have been awarded have been determined, with one exception, chiefly by preferences of the donors, though the Council has of course assured itself that the preferred recipients were competent and that the plans of work submitted by them were adequate and satisfactory. The one exception has been a grant to Dr. Stoke's clinic for a study of the absorption of sugars which would enable them to continue a promising research already in progress.

The plan for a large-scale study of the adolescent child discussed at the time of our last report has still not reached the point of definite decision. After a conference between Dr. Gregg of the Rockefeller Foundation, Dr. Stuart, and myself, it was left for further consideration by the Foundation. The Council is being consulted more frequently as time goes on regarding various projects germane to its field, some of which might involve grants for research to be allocated through the Council, while others will require perhaps only the giving of advice regarding proper approach to particular problems or proper agencies to be consulted.

The Council has not spent the grant from the Carnegie Corporation quite so rapidly as was originally contemplated. There remains, with fees received and receivable, enough in its bank account to carry it to approximately October 1, 1939. We are committed to see through some researches which will extend beyond that period. We have no present means of knowing whether we shall, during the time between now and October, receive grants involving fees which will carry us for any considerable further period. We think that our present progress is encouraging and that it is likely that our receipts from now on will be greater rather than less, but we have not at present any definite assurance as to how we may be able to finance ourselves during the possible—even probable—hiatus between the first of October and the time of further receipts.

A report has been submitted to the Carnegie Corporation covering all of these points.

Respectfully submitted,

THOMAS B. COOLEY, Executive Secretary

News and Notes

Oliver W. Hill

Oliver Hill of Knoxville, Tenn., died June 21 of cardiac disease. He was 57 years of age. Dr. Hill was the pioneer pediatrician in his city and region, and had been prominent in pediatric and medical activities for 30 years. He was responsible for the establishment of the Home for Friendless Babies in Knoxville and had been the physician in charge for many years. Dr. Hill was a Founder of the Academy and a regular attendant at pediatric meetings. He was actively interested in Academy affairs and at the time of his death was a member of the Committee on Contact Infections.

The **Eighth Pan-American Child Congress** will be held Oct. 12-19, 1939, at San Jose, Costa Rica. There will be sections and sectional meetings on medical

pediatric problems, surgical problems, law and sociology, child hygiene, education, and social welfare. In addition to official delegates appointed by the governments of the various countries in the Pan-American Union, membership is open to pediatricians. They may present reports on the subjects chosen for discussion and take part in discussions. The official languages will be Spanish, English, French and Portuguese. The subjects designated for Section I, medical pediatric problems, are as follows:

Official Subjects:

1. Hydrosaline metabolism in digestive disorders of the infant.
2. Vitamin deficiencies in children in the tropics.
3. Blood transfusion in pediatrics.

Recommended Subjects:

1. Treatment of toxicosis in the infant by the method of continuous intravenous instillation.
2. Value of clinical and radiologic data in cardiac disease in children.
3. Treatment of bronchopneumonia in children.
4. Perivascular forced (spinal) drainage in poliomyelitis and chorea.
5. Treatment of acute enterocolitis in children with diathermy or ultrashort waves.

Among subjects to be considered under surgical pediatric problems are acute abdominal conditions, osteomyelitis, and birth injuries; in the child hygiene section, vaccines for whooping cough, control of poliomyelitis, and control of tuberculosis.

More detailed information may be obtained from the Children's Bureau, in Washington, D. C., which has issued a special bulletin of the regulations.

An Institute for the consideration of the blood and blood-forming organs will be held at the Medical School of the University of Wisconsin, Madison, Wisconsin, September 4th to 6th inclusive. Papers and round tables will make up the program. Included among the speakers are Dr. George R. Minot of Boston, Dr. L. J. Witts of Oxford and Dr. Meulengracht of Copenhagen.

The **American Board of Pediatrics** announces the following dates for examinations in 1940.

New York City—April 30 and May 1.

Kansas City, Mo.—The day preceding the meeting of Region III of the American Academy of Pediatrics.

Seattle—The day preceding the meeting of Region IV of the American Academy of Pediatrics.